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CONTENTS [illegible] PREVI[illegible] NUMBER

OCTOBER 1934

The [illegible] Control [illegible]
[illegible] Donald [illegible]
[illegible] Kroger, [illegible]
delphia

Uterine [illegible] in Women. Their [illegible]
Howard [illegible] and Morris A. [illegible], M.D.
Chicago

Iodids Therapy for Relief of Pain in [illegible]
Russell [illegible] Brauer, M.D.
[illegible], M.D. New York

Ulcus Vulvae Acutum; Accompanied by Disse[illegible]
M. [illegible] and Myron Moscow, [illegible]
M.D., [illegible], U. S. A. R.

Differential Diagnosis of Hymenial Seline [illegible]
[illegible] Especially. C. C. Carpenter, M.D.
Seattle

Tuberculosis of the Stomach Nothing Gut
W. [illegible], M.D. Minneapolis

Epithelioma: Radical Acquisitio Successful
Treatment [illegible] Iron Coagulation, Radio
Generation, [illegible] Fulguration, and
Roentgen Ray. Herman A. Schmidt, M.D.
Philadelphia, Pa.

Duodenal Hydrocele Associated with Congenital
[illegible] Tobias, M.D., St.
Louis

Dermatitis [illegible] Lenticularis Disseminata. [illegible]
[illegible] Hazen, Okmulgee, Okla.

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Archives of Dermatology and Syphilology

VOLUME 30 NOVEMBER 1934 NUMBER 5

SPECIFICITY OF A STREPTOCOCCUS ISOLATED FROM PATIENTS WITH PEMPHIGUS

PRELIMINARY REPORT

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ROCHESTER, MINN.

This report deals with bacteriologic studies of the blood, of material obtained from the nasopharynx and of the fluid from blisters of seven patients who had pemphigus. A streptococcus was isolated from the blood of five of the patients in each of ten trials, whereas cultures from the blood of a sixth patient with pemphigus were sterile on four separate occasions. A characteristic streptococcus was isolated from swabbings of the nasopharynx of these seven patients in each of the twenty-one attempts. A similar streptococcus was obtained from the fluid of blisters only once in thirty-four trials.

METHOD OF ISOLATING THE STREPTOCOCCUS FROM THE BLOOD

Blood for culture was drawn in amounts of 20 cc. as aseptically as possible and put into sterile tubes containing 5 cc. of a 2 per cent solution of sodium citrate in a physiologic solution of sodium chloride. From 4 to 5 cc. of the mixture was added to Rosenow's dextrose-brain broth medium in tall tubes measuring 1.5 by 20 cm.[1] After inoculation half of these tubes were fused in an oxygen flame to sterile long glass tubes, exhausted with a vacuum pump and then sealed off, thus producing tall anaerobic ampules. The remainder of the inoculated tubes were simply closed with cotton plugs. The anaerobic and partial tension tubes were incubated at 35 C.

Clouding and a pink tinge appeared first at the bottom of the anaerobic tubes; later, in most instances within from twenty-four to forty-eight hours, the clouding became diffuse. In every instance the tubes that were not exhausted and hermetically sealed remained clear.

Blood obtained in the same manner was also injected intraperitoneally into full-grown white mice in amounts of 4 cc. Mice which received injections of blood from four of the five patients with pemphigus from whom positive blood cultures were obtained in the anaerobic tubes of dextrose-brain broth died within approximately eight hours. Blood from the fifth patient with pemphigus from whom positive blood cultures were obtained was not injected into mice. Of the six

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From the Section on Dermatology and Syphilology, the Mayo Clinic.

Read before the Section on Dermatology and Syphilology at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 13, 1934.

1. Rosenow, E. C., and Jensen, L. B.: Cataphoretic Velocity of Streptococci Isolated in Cases of Encephalitis and of Other Diseases of the Nervous System, J. Infect. Dis. **52**:167 (March-April) 1933.

mice which received injections of blood from the patient with pemphigus whose blood cultures were negative, none died. Partial tension and anaerobic cultures in dextrose-brain broth were made from the bloody peritoneal contents of the mice that succumbed. These cultures were incubated at 35 C. Clouding and a pink color appeared in from eighteen to twenty-four hours in both the anaerobic and the partial tension tubes. Mice receiving similar injections of blood from eight normal people and from ten patients who had other types of dermatosis lived and, after observation for one month, were killed.

METHOD OF ISOLATING THE STREPTOCOCCUS FROM THE NASOPHARYNX

The nasopharynx was swabbed in the manner described by Rosenow.[2] The swabs were placed in tubes containing 2 cc. of gelatin (0.2 per cent) Locke's solution, and the tubes were thoroughly agitated. Blood agar plates and tubes of dextrose-brain broth were inoculated from the swabs and then incubated for eighteen hours at 35 C. Clouding appeared first in the bottom of the dextrose-brain broth tubes; it gradually became diffuse, and a pink color appeared. The blood agar plates were examined after from twelve to twenty-four hours of incubation.

The mixed dextrose-brain broth cultures from the nasopharynx were purified as follows: Rabbits received intracerebral injections of 0.2 cc. of the dextrose-brain broth cultures from the nasopharynx which had been incubated for from eighteen to twenty-four hours. These animals died in from twelve to twenty-four hours. After death the cranial cavities were opened as aseptically as possible, and purulent meningitis, marked congestion of the cerebral and meningeal vessels and a diffuse inflammatory process in the brain tissue (meningo-encephalomyelitis) were found. Cultures were made from the brains on blood agar plates and in partial tension tubes of dextrose-brain broth.

METHODS OF ISOLATING THE STREPTOCOCCUS FROM THE BLISTER FLUID

The surface of the skin was prepared as for taking blood for culture. The bullae were punctured by sterile capillary pipets, into which the fluid was drawn. With the blister fluid thus obtained, blood agar plates, tubes of brain broth and Kendall's K mediums [2a] were inoculated. These were incubated at 35 C. for one month and examined daily.

DETERMINATIONS OF CATAPHORETIC MOBILITY

Determinations of cataphoretic mobility were made on the fresh dextrose-brain broth cultures of the streptococcus obtained from the blood and nasopharynges of patients who had pemphigus, as originally

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2. Rosenow, E. C.: Cataphoretic Time and Velocity of Streptococci and Pneumococci. Studies on Organisms Isolated in Cases of the Common Cold, Influenza, Bronchopneumonia and Lobar Pneumonia, J. Infect. Dis. **54**:91 (Jan.-Feb.) 1934.

2a. Kendall: Mediums for the Isolation and Cultivation of Bacteria in the Filtrable State, Northwestern University Bull. 8, 1931, vol. 32.

isolated and after passage through animals, by means of the Northrop-Kunitz-Mudd apparatus, the technic described by Rosenow [3] being used.

This apparatus consists essentially of a microscope focused on the neutral layer of a flat glass cell of constant vertical diameter connected through glass tubes at each end with nonpolarizable zinc electrodes. A screen composed of identical squares is contained in the ocular, so that one sees the grating of the screen superimposed on the bacteria in focus in the microscopic field. When the electrical circuit is completed, bacteria suspended in the cell, being negatively charged, move toward the anode at different mobilities. The organisms are timed with a stop-watch across two squares, or a distance of 48.1 microns. The actual mobility is derived from these readings by use of the following formula:

$$M \text{ (mobility)} = \frac{d \text{ (distance, 48.1 cm., over which organism is timed)}}{t \text{ (time in seconds)}} \cdot \frac{v \text{ (effective voltage between the electrodes)}}{d \text{ (distance between the platinum electrodes at each end of cell between which the effective voltage is measured)}}$$

Rosenow,[4] Rosenow and Jensen [5] and others have demonstrated that green-producing streptococci which have elective localization for the central nervous system, an ectodermal structure, have a cataphoretic mobility of either 1.72 or 3.45. As is illustrated in figure 1, the two peaks in the mobility distribution curve of the streptococci which were isolated from the blood and nasopharynges of patients who had pemphigus are at the same two points (1.72 and 3.45) on isolation and after passage through animals.

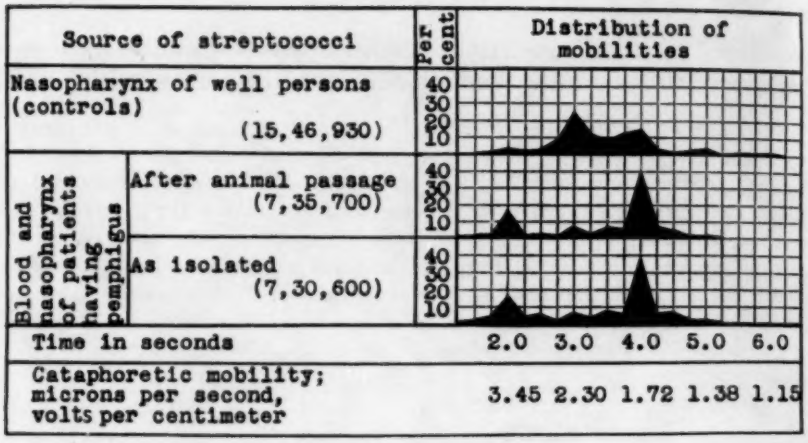
MORPHOLOGY OF THE ORGANISM

The organism isolated from these patients with pemphigus is extremely pleomorphic. In the primary culture from the blood it usually appeared as a streptococcus (fig. 2 *a*), but in some cultures pleomorphic forms, consisting of a mixture of ovid, coccoid and bacillary forms, and in still other cultures bacillary forms only were obtained (fig. 2 *b*). In dextrose-brain broth cultures from the nasopharynx, only the streptococcic form was found. Early transplants on blood agar plates from the dextrose-brain broth cultures from the nasopharynx and from primary cultures on blood agar plates produced colonies which were indistinguishable from one another but which on smearing in some instances revealed pure streptococcic forms, in other instances a mixture

3. Rosenow, E. C.: (*a*) Cataphoretic Velocity and Virulence of Streptococci Isolated from the Nasopharynx of the Same Person While Well and During Attacks of Epidemic Gastro-Enteritis, of Sore Throat, and of Influenza, Proc. Staff Meet., Mayo Clin. **8**:6 (Jan. 4) 1933; (*b*) Cataphoretic Velocity of Streptococci as Isolated in Studies of Arthritis, Arch. Int. Med. **51**:327 (March) 1933. Rosenow.[2]

4. Rosenow and Jensen.[1] Rosenow.[2 3b]

5. Rosenow, E. C., and Jensen, L. B.: Elective Localization and Cataphoretic Potential of Streptococci, Proc. Soc. Exper. Biol. & Med. **27**:442 (Feb.) 1930.



*The figures in parenthesis indicate respectively, the number of strains, cultures, and streptococci timed in each group.

Fig. 1.—The cataphoretic time and mobility of streptococci isolated from the blood and nasopharynx of patients suffering from pemphigus.

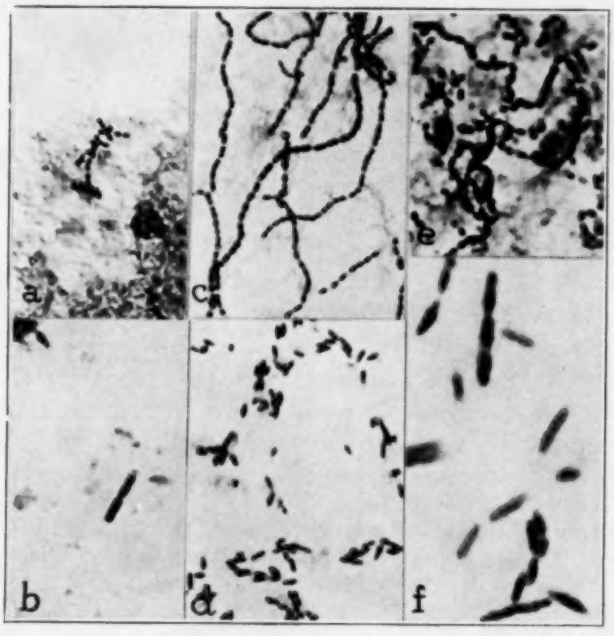


Fig. 2.—The pleomorphism of the streptococcus isolated from patients with pemphigus. The various forms are: (*a*) streptococcic, (*b*) bacillary (in primary isolation from the blood of patient 38), (*c*) streptococcic, (*d*) bacillary, after passage through animals, (*e*) bacillary and coccal, in the same chains, and (*f*) granules or coccoid bodies inside the bacillary forms.

of coccoid and baclilary forms and in still others only bacillary forms. Some of the pleomorphic forms revealed a tendency toward clubbing and were diphtheroid in appearance. The stable form is the streptococcic form. Subculturing several times in dextrose-brain broth, heating followed by a single subculture in dextrose-brain broth and often passage through animals served to convert the pleomorphic forms to the stable streptococcic form (fig. 2 *c*). In a few instances, however, young pleomorphic, bacillary (fig. 2 *d*) and diphtheroid forms survived passage through animals without conversion to the streptococcic form. Smears from some cultures in dextrose-brain broth revealed bacillary and coccoid forms in the same chain (fig. 2 *e*). Smears of colonies on blood agar plates, when more than twenty-four hours old, often revealed coccoid bodies or granules inside the bacillary forms (fig. 2 *f*). Immunologically and antigenically, all forms behaved identically. The aforementioned changes in morphologic characteristics are consistent with those observed in other streptococci by Rosenow,[6] Jensen and Morton,[7] Mellon [8] and Koch and Mellon.[9]

STAINING REACTIONS

The organism stains satisfactorily with the usual aniline dyes. It is definitely gram-positive and is decolorized with relative difficulty. It is not acid-fast. In old cultures, shadow forms appear, and when the organisms are stained by Gram's method, considerable decolorization takes place on moderate washing in alcohol.

CULTURAL CHARACTERISTICS

The organism is an obligate anaerobe when first isolated from the blood, but it grows equally well at partial oxygen tension and anaerobically when isolated from the nasopharynx. It grows best in Rosenow's dextrose-brain broth. In this medium, growth first appears at the bottom of the tube and later becomes fairly diffuse. Sediment, if present, is flocculent. Partial tension strains from the nasopharynx grow rapidly on blood agar plates, whereas freshly isolated anaerobic strains from

6. Rosenow, E. C.: The Etiology and Experimental Production of Erythema Nodosum, J. Infect. Dis. **16**:367 (May) 1915.

7. Jensen, L. B., and Morton, H. B.: The Diphtheroid Phase of Streptococci, J. Infect. Dis. **49**:425 (Nov.) 1931.

8. Mellon, R. R.: A Study of the Diphtheroid Group of Organisms with Special Reference to Its Relations to the Streptococci: II. Classification of the Diphtheroid Group, J. Bact. **2**:269 (May) 1917; The Life-Cycle Changes of the So-Called C. Hodgkini and Their Relation to the Mutation Changes in This Species, J. M. Research **42**:61 (July-Sept.) 1920.

9. Koch, R., and Mellon, R. R.: The Biological and Clinical Significance of Diphtheroids in the Blood Stream, J. Bact. **19**:25 (Jan.) 1930.

the blood are difficult to start unless they are first transplanted several times in dextrose-brain broth. On isolation, colonies on blood agar plates are from two to three times the size of colonies of the green-producing and indifferent streptococci usually found in throats. The colonies are somewhat irregular in outline and have a smooth surface; they are flat, glistening, translucent and of butyroid consistency, and they produce a wide, intensely green zone. After a few subcultures, the characteristics of these colonies on blood agar plates change and they become indistinguishable from those of the streptococci usually present in throats. The organism will not grow in plain broth or on plain agar plates. It is not bile-soluble. Optimal growth occurred at 35 C.

TABLE 1.—*Fermentation Reactions*

	Source of Streptococci				
	Pemphigus			Dermatitis Herpetiformis (Control);	Lupus Erythematosus (Control);
Sugars	Single Strain (Case 19)	Single Strain (Case 14)	Pool of Nineteen Strains	Pool of Four Strains	Pool of Seven Strains
Dextrose	+	+	+	+	+
Maltose	+	+	+	+	+
Mannitol	+	+	+	—	—
Sucrose	+	+	+	+	+
Levulose	+	+	+	+	+
Lactose	+	+	+	+	+
Galactose	+	+	+	+	+
Salicin	+	+	+	+	—
Raffinose	—	—	—	+	+
Inulin	—	—	—	—	+
Arabinose	—	—	—	—	+
Xylose	—	—	—	—	+
Dulcite	—	—	—	—	+
Inosite	—	—	—	—	+

FERMENTATION REACTIONS

The fermentation reactions of the organism are recorded in table 1. Each of two single strains and a pool of nineteen strains are shown to ferment the same sugars. The fermentation reactions of the control streptococci from patients who had dermatitis herpetiformis and lupus erythematosus are different.

The medium for the fermentation tests was prepared by mixing 1,000 cc. of distilled water, 10 Gm. of peptone (Witte's) and 5 Gm. of sodium chloride and by heating the mixture until the solids were dissolved. The solution was filtered, and 10 cc. of 0.2 per cent alcoholic bromthymol blue was added. The solution was then tubed in amounts of 5 cc., and the tubes were placed in the autoclave for twenty minutes at 20 pounds (9.1 Kg.) of pressure. Sugars were made up in a 10 per cent solution and filtered (Seitz' method) to sterilize them, and 0.25 cc. was added to each of the tubes just mentioned. Inoculated tubes were incubated at 35 C. for forty-eight hours and then read.

INJECTION INTO ANIMALS

The organism was injected into two hundred and seven mice, rats, guinea-pigs and rabbits. It was virulent, producing death in from eight to twenty-four hours in all the four species, regardless of the route of injection, when the amounts given were comparable to those of other streptococci usually given to the same animals by the same routes. White mice were especially susceptible. When smaller amounts were given intracerebrally, all the animals died within forty-eight hours, and when the injections were given by other routes, about 75 per cent of the animals died in from four to five days. The remainder lived from three to four weeks. In the group that lived only four or five days, more than 30 per cent gave evidence of purulent conjunctivitis with or without ulceration, purulent vaginitis, phimosis, paraphimosis with or without ulceration and diarrhea; these findings occurred singly or in various combinations. The characteristic lesion in mice was purulent conjunctivitis, often with ulceration and adhesion of the lids. Smears from the purulent exudate of the eyes of all the animals uniformly disclosed no bacteria. Among several guinea-pigs, areas of gangrene in the skin remote from the sites of injection also developed. Among a few rabbits, bullous lesions were found on the conjunctiva and on mucous membranes of the foreskin and mouth. In the group that lived from three to four weeks, postmortem examination revealed extreme emaciation, toxic changes in all the organs, splenomegaly, general lymphadenopathy, congestion of the cerebral and meningeal vessels and, in a small percentage, some of the lesions of the mucous membrane just described. Cultures from the organs of the animals of this group were uniformly negative, whereas the organism was recovered from all the other animals. Intradermal injections of the organism into rabbits and guinea-pigs produced large, indolent abscesses, with much induration and erythema, in contrast to the small, transient lesions produced by comparable injections of green-producing streptococci from patients who had arthritis or encephalitis and from those with normal throats.

Chronic foci were produced in guinea-pigs and rabbits by intratibial injections of small amounts of the dextrose-brain broth cultures of the streptococcus and by the introduction into the peritoneal cavity through a paracentesis needle of cotton plugs soaked in dextrose brain-broth cultures of the streptococcus, as described by Moon and Konzelmann.[10] Injections were also made into the anterior chamber of the eye.

After from one to two weeks, more than 75 per cent of the animals with chronic foci, on subsequent injection of the streptococcus, revealed various combinations of the lesions previously described, and, in addi-

10. Moon, V. H., and Konzelmann, F. W.: A Method of Producing Chronic Focal Infections, Arch. Path. **10**:587 (Oct.) 1930.

tion, a small percentage gave evidence of bullous lesions of the skin, conjunctiva, foreskin and the mucous membranes of the mouth. Intradermal injections of the killed organism into guinea-pigs and rabbits which had chronic foci containing the same organism produced large areas of inflammatory reaction, some with bullous lesions and hemorrhage, whereas intradermal injections of control green-producing streptococci from patients with other cutaneous and systemic diseases produced little reaction.

The one monkey which received injections was given a small intratibial injection of a dextrose-brain broth culture of the streptococcus, followed by a second injection fifteen days later. It died three days after the last injection and at postmortem examination revealed a bullous lesion of the mucous membrane of the right side of the upper jaw, a superficial ulcer with little inflammatory reaction in the groove between the jaw and the cheek on the lower right side, hemorrhagic bullous lesions of the conjunctivae, many small superficial ulcers in the stomach and colon, toxic changes in all the organs and emaciation.

Lesions of these types were observed in less than 2 per cent of the animals that were given injections of cultures of the streptococcus which were more than 72 hours old, of cultures in which the organism had become saprophytic after several subcultures on artificial mediums or of control streptococci from patients with other cutaneous and systemic diseases.

INTRADERMAL AND SUBCUTANEOUS INJECTION OF DEAD ORGANISMS INTO PATIENTS WITH PEMPHIGUS

Suspensions of the organisms killed by heat, formaldehyde solution or by hydrochloric acid were injected intradermally and subcutaneously into three patients with pemphigus. Bullous lesions, rarely accompanied by inflammatory reaction, appeared in from eight to twelve hours at the sites of intradermal and subcutaneous injections (fig. 3). In one case two large bullae with surrounding erythema were produced by intradermal injection of two different strains of the organisms. When the patient was given subsequent injections of suspensions of the killed organisms intradermally or subcutaneously in the opposite arm, new bullae appeared within eight hours at the two sites of previous injection of the dead organisms. This phenomenon was repeatedly demonstrated weeks after the original skin tests. Large doses of vaccine made from the organisms when injected subcutaneously into the patient produced crops of new bullae in areas formerly occupied by lesions, as well as crops of new lesions in previously uninvolved areas.

Control injections of dead green-producing streptococci from patients who had other cutaneous and systemic diseases failed to produce any of the phenomena just described.

Intradermal injections of the dead streptococci from patients with pemphigus into normal persons and patients with other cutaneous diseases failed to produce bullae.

Intramuscular injections of an antibody globulin solution obtained from the serum of a horse which had been immunized in the manner described by Rosenow [11] to a mixture of seven strains of the streptococcus produced a severe, widespread crop of small bullae in the only patient to whom it was given.

EXPERIMENTS TO ESTABLISH THE IDENTITY OF THE INDIVIDUAL STRAINS [12] OF THE STREPTOCOCCUS

Agglutination Reactions with Immune Horse and Immune Rabbit Serums.—The titer of agglutinins in the serums from patients who had pemphigus was found to be insufficient to demonstrate clearly cross-agglutination of the different strains of the streptococcus. Therefore,

Fig. 3.—Lesions *1* to *9* are bullae without erythematous bases produced by intradermal injection into a patient with pemphigus of individual strains of the specific streptococcus. Numbers *10* to *12* are sites of control injections of other streptococci.

each of thirteen rabbits was immunized with a single strain, and a horse was immunized with a mixture of seven strains.

The immune rabbit serums were prepared as follows: Suspensions of the streptococcus in a 0.9 per cent solution of sodium chloride, four times the density of a dextrose-brain broth culture, were made from the dense stock suspension in glycerin (2 parts) and 25 per cent sodium chloride solution (1 part) which had been kept in the refrigerator, and the organisms were killed by the addition of a

11. Rosenow, E. C.: Serologic Specificity of Streptococci Having Elective Localizing Power as Isolated in Various Diseases of Man, J. Infect. Dis. **45**: 331 (Nov.) 1929; An Institutional Outbreak of Poliomyelitis Apparently Due to a Streptococcus in Milk, ibid. **50**:377 (May-June) 1932.

12. In order to avoid confusion, the word "strain" in the remainder of this paper is applied to each of the thirty-two individual pure cultures of the organism isolated from the blood, nasopharynx and blister fluid of the seven patients who had pemphigus. It is used in the same manner in referring to streptococci isolated from patients with other diseases.

0.05 per cent solution of formaldehyde. These antigens were given intravenously on three successive days each week for six weeks, in doses of 1, 2 and 3 cc. the first week, 3, 4 and 5 cc. the second week, and so on until a dose of 10 cc. was reached. The animals were then allowed to rest two weeks, after which they were bled to death from the carotid artery.

The suspensions of streptococci for agglutination tests were made from the dense stock suspensions. The dense suspensions were diluted in distilled water to about one-fourth the density of a dextrose-brain broth culture, or to about 500,000,000 streptococci per cubic centimeter and used directly. The set-ups were kept at 35 C. for one and one-half hours, and then placed in the refrigerator over night. Readings were made on removal from the incubator and again the following morning.

As is indicated in table 2, each of the immune rabbit serums and the immune horse serum agglutinated to some degree all, and to a marked degree most, of the sixteen strains of the streptococcus isolated from patients who had pemphigus, but failed to agglutinate the control streptococci, consisting of three individual strains from patients who had lupus erythematosus, a pool of three strains from patients who had dermatitis herpetiformis and a pool (5418 [13]) of six strains from patients who had arthritis.

Agglutinin-Absorption in Pooled Immune Rabbit and Immune Horse Serums.—After demonstrating cross-agglutination with each immune rabbit serum, a pool was made containing equal quantities of all thirteen serums.

Serums for absorption were diluted 1:10. Suspensions of the organisms for absorbing were made from the dense stock suspensions about four times the density of a dextrose-brain broth culture. Incubation was carried out at 35 C. for one and one-half hours, and the organisms were removed from the serum by centrifugation. After the serum had been thus treated it was diluted further and used for agglutination tests and for determinations of streptococcus mobility in serum.

In table 3 it is shown that by the absorption of the pooled immune rabbit serum and of the immune horse serum with a single strain of the streptococcus isolated from a patient with pemphigus the agglutinins for all the sixteen strains which previously were shown to be agglutinated by the serums were removed from them. Absorption of the pooled immune rabbit serum with a pool (104) of seven strains of streptococci from patients who had lupus erythematosus and of the immune horse serum by a pool of four strains of streptococci isolated from patients who had dermatitis herpetiformis failed to show removal of the agglutinins for any of the sixteen strains of streptococci derived from patients who had pemphigus; the serums thus treated acted exactly

13. This suspension of streptococci and the suspension of streptococci (7593) from patients who had encephalitis were given to me by Dr. E. C. Rosenow.

TABLE 2.—*Individual Serums from Thirteen Rabbits Immunized with Single Strains, and the Serum of a Horse Immunized with a Mixture of Seven Strains, Agglutinate Sixteen Strains of the Streptococcus*

Antigens	Strain	Individual Serums from Rabbits Immunized to Single Strains of Streptococci Isolated from Patients Who Had Pemphigus (Dilution 1:20)													Serum of Immune Horse 97*	Controls		
		1	2	3	4	5	6	7	8	9	10	11	12	13		Serum of Normal Horse (1:20)	Serum of Normal Rabbit (1:20)	Salt Solution
Individual strains of streptococci isolated from patients who had pemphigus	1	1+	2+	4+	4+	3+	2+	2+	2+	1+	1+	1+	2+	3+	1+	—	—	—
	2	3+	4+	4+	4+	4+	4+	4+	4+	3+	4+	3+	3+	4+	4+	—	—	—
	3	3+	4+	4+	4+	4+	3+	3+	3+	3+	2+	2+	2+	3+	4+	—	—	—
	4	3+	2+	3+	3+	4+	3+	4+	4+	4+	3+	4+	4+	3+	1+	—	—	—
	5	4+	4+	4+	4+	4+	3+	4+	4+	4+	2+	4+	4+	4+	3+	—	—	—
	6	2+	1+	2+	1+	2+	1+	1+	1+	1+	3+	2+	1+	1+	1+	—	—	—
	7	1+	4+	4+	2+	3+	3+	3+	4+	2+	2+	3+	3+	3+	4+	—	—	—
	8	1+	1+	3+	3+	3+	1+	3+	3+	2+	2+	3+	2+	3+	3+	—	—	—
	9	1+	3+	4+	3+	2+	2+	1+	3+	2+	2+	3+	3+	1+	3+	—	—	—
	10	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	1+	—	—	—
	11	1+	1+	4+	2+	1+	1+	1+	3+	2+	2+	1+	1+	1+	3+	—	—	—
	12	3+	3+	4+	2+	2+	2+	1+	3+	2+	2+	3+	3+	3+	3+	—	—	—
	13	1+	3+	4+	4+	3+	4+	3+	3+	2+	3+	3+	4+	3+	3+	—	—	—
	14	4+	4+	4+	4+	4+	4+	4+	4+	4+	4+	4+	4+	4+	4+	—	—	—
	15	2+	1+	3+	3+	3+	2+	3+	4+	2+	2+	1+	2+	1+	4+	—	—	—
	16	2+	2+	4+	3+	3+	3+	3+	4+	2+	2+	1+	2+	2+	3+	—	—	—
Individual strains of streptococci isolated from patients who had lupus erythematosus	7	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	6	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Pool of three single strains of streptococci isolated from patients who had dermatitis herpetiformis.....	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Pool of six strains of streptococci isolated from patients who had arthritis	5418	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—

* The horse was immunized with a mixture of seven strains from patients who had pemphigus.

TABLE 3.—*Agglutinin-Absorption Reactions. Absorption from Immune Rabbit Serum and Immune Horse Serum of Agglutinins for Sixteen Strains of Streptococci Isolated from Patients Who Had Pemphigus, by Single Strains of Streptococci from Same Source*

		Rabbit Serum (1:20)				Horse Serum (1:20)				
Antigen	Strain	Pooled Normal	Pooled Immune Untreated	Pooled Immune Absorbed by Strain 1 from Pemphigus	Pooled Immune Treated with Strain 104 from Lupus Erythematosus	Normal Horse	Horse 97, Immunized with Seven Strains from Pemphigus	Horse 97, Serum Absorbed by Strain 1 from Pemphigus	Horse 97, Serum Treated with Pool of 7 Strains from Dermatitis Herpetiformis	Salt Solution Control
Individual strains of streptococci isolated from patients who had pemphigus	1	—	3+	—	3+	—	4+	—	4+	—
	2	—	2+	—	2+	—	4+	—	4+	—
	3	—	2+	—	2+	—	4+	—	4+	—
	4	—	4+	—	4+	—	4+	—	4+	—
	5	—	4+	—	4+	—	4+	—	4+	—
	6	—	1+	—	1+	—	4+	—	4+	—
	7	—	4+	—	4+	—	4+	—	4+	—
	8	—	3+	—	3+	—	4+	—	4+	—
	9	—	4+	—	4+	—	4+	—	4+	—
	10	—	1+	—	1+	—	4+	—	4+	—
	11	—	4+	—	4+	—	4+	—	4+	—
	12	—	4+	—	4+	—	4+	—	4+	—
	13	—	4+	—	4+	—	4+	—	4+	—
	14	—	3+	—	3+	—	3+	—	3+	—
	15	—	4+	—	4+	—	4+	—	4+	—
	16	—	4+	—	4+	—	4+	—	4+	—
Pool of nineteen strains	102	—	4+	—	4+	—	4+	—	4+	—
Pool of seven strains of streptococci isolated from patients who had lupus erythematosus	104	—	—	—	—	—	—	—	—	—
Pool of seven strains of streptococci isolated from patients who had dermatitis herpetiformis	103	—	—	—	—	—	—	—	—	—
Pool of six strains from patients who had arthritis	5418	—	—	—	—	—	—	—	—	—

TABLE 4.—*Positive Precipitin Reactions Between Cleared Nasopharyngeal Washings and Serums of the Horse and of Rabbits Immunized with the Streptococcus from Patients Who Had Pemphigus*

			Incidence of Positive Reactions in Serums				
Source of Nasopharyngeal Washings	Cases	Tests	Horse 97 Immunized with the Streptococcus from Pemphigus	Horse 96 Immunized with the Streptococcus from Encephalitis	Rabbits (175 to 187) Immunized with the Streptococcus from Pemphigus (Pooled)	Normal Horse	Normal Rabbit (Pooled)
Pemphigus	7	20	17 (85%)	1 (5%)	16 (80%)	0	0
Lupus erythematosus	6	8	0	0	0	0	0
Dermatitis herpetiformis	6	7	0	0	0	0	0
Erythema multiforme	3	3	0	0	0	0	0
Other skin diseases: herpes zoster, pityriasis rosea, lichen planus, etc.	16	18	1 (5.5%)	3 (16.6%)	2 (11%)	0	0

as did untreated serums. Absorption of the agglutinins from these immune serums was demonstrated with eight other individual strains of the organism derived from patients who had pemphigus.

PRECIPITIN REACTIONS

Tests for precipitin reactions between the cleared nasopharyngeal washings from patients who had pemphigus and the immune horse and pooled immune rabbit serums were performed after the method described by Rosenow.[14] As is shown in table 4, positive reactions were obtained in seventeen, or 85 per cent, of the twenty tests made with the immunized horse serum and in sixteen, or 80 per cent, of the twenty tests made with the pooled immune rabbit serum. The serum of a horse which had been immunized by Rosenow [11] with streptococci from patients who had encephalitis gave a positive reaction in only one (5 per cent) of twenty tests with the nasopharyngeal washings from patients who had pemphigus. All three immune serums gave negative reactions with control nasopharyngeal washings from patients who had lupus erythematosus, dermatitis herpetiformis and erythema multiforme, and only a low percentage of positive reactions with nasopharyngeal washings from sixteen patients who had other skin diseases.

CATAPHORETIC MOBILITY OF THE STREPTOCOCCUS IN IMMUNE SERUM

It has been shown by Rosenow,[15] Rosenow and Jensen, Shibley,[16] Mellon and Grenquist,[17] Thompson [18] and others that the cataphoretic mobility of streptococci is markedly reduced when these organisms are treated with serums containing antibodies specific for them. The cataphoretic mobility of the streptococcus from patients with pemphigus was

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14. Rosenow, E. C.: A Specific Precipitin Reaction in Epidemic Poliomyelitis, J. A. M. A. **84**:429 (Feb. 7) 1925; The Precipitin Reaction in the Diagnosis of Scarlet Fever and Allied Hemolytic Streptococcus Infections, ibid. **86**:9 (Jan. 2) 1926.

15. Rosenow, E. C.: A Specific Reaction of Convalescent Serum on the Streptococcus Isolated in Studies of Poliomyelitis, J. Immunol. **23**:455 (Dec.) 1932. Rosenow.[2,3] Rosenow and Jensen.[5]

16. Shibley, G. S.: Studies in Agglutination: II. The Relationship of Reduction of Electrical Charge to Specific Bacterial Agglutination, J. Exper. Med. **40**: 453 (Oct.) 1924; Studies in Agglutination: III. On the Mechanisms of the Agglutination of Bacteria by Specific Agglutinating Serum, ibid. **44**:667 (Nov.) 1926.

17. Mellon, R. R., and Grenquist, Ernst: Studies in Microbic Heredity: IV. Observations on Group Agglutinins in Specific Sera with the Technic of Cataphoresis, J. Immunol. **11**:161 (Feb.) 1926.

18. Thompson, R. L.: Electrophoresis of Organisms Belonging to the Pneumococcus Group, A. J. Hyg. **14**:244 (Sept.) 1931.

determined in immune rabbit serum, immune horse serum and serum of man.

The suspensions of the respective strains of the streptococcus were made as for agglutination reactions, but were diluted in triple distilled water to about one-eighth the density of a dextrose-brain broth culture, or to about 250,000,000 streptococci per cubic centimeter, and used directly. One cubic centimeter of this dilute suspension of streptococci and 1 cc. of the diluted serum, and a control of 1 cc. of the suspension and 1 cc. of a sodium chloride solution (0.9 per cent) were put in chemically clean test tubes and thoroughly shaken. The set-ups were kept at 35 C. for one hour and a half and at room temperature (from 20 to 24 C.) for one hour; the content of each tube was then diluted to 10 cc. with distilled water, poured into the cataphoresis cell and read in the usual way. Not more than ten tubes were put in one set-up, since, if more were added, before all of them could be read the difference in the time at room temperature between the first and last tubes would be so great that the readings could not be regarded as comparable.

As is indicated in table 5, the serum of one rabbit (185) which was immunized with only one strain and the serum of a horse which was immunized with a mixture of seven strains of the streptococcus from pemphigus reduced the mobility of eighteen strains from the same source an average of 61 and 50 per cent, respectively, as compared with their average mobility in a solution of sodium chloride. The control normal rabbit and normal horse serums reduced the average mobility of these same strains an average of 16 and 15 per cent, respectively. The same immune serums reduced the mobility of the control streptococci obtained in a study of five other diseases only a little more than normal rabbit and normal horse serums did. The serums of twelve other rabbits, each immunized with a single strain of the streptococcus from pemphigus, gave similar results.

In the four typical reactions with serums of man (table 5) it will be seen that serum from one patient who had pemphigus, from one who had lupus erythematosus, from one who had dermatitis herpetiformis and from one who had erythema multiforme reduced the cataphoretic mobility of the respective streptococci, compared with the average mobility in a solution of sodium chloride, an average of 65, 45, 60 and 51 per cent, respectively. The effect of each serum on the control streptococci for that serum was little more than the effect of normal serum. The average reduction of the mobility of the streptococci from patients with each disease was about the same in each nonspecific serum.

The serum from twelve patients with the four diseases named (three patients representing each disease) gave similar results with the same antigens.

TABLE 5.—*Reduction of the Mobility of the Streptococci Isolated from Patients Who Had Pemphigus: (1) by the Serum of a Rabbit Immunized with One Strain; (2) by the Serum of a Horse Immunized with a Mixture of Seven Strains and (3) by the Serum of a Patient Who Had Pemphigus*

Source of Streptococci	Strains	Average Mobility in Salt Solution (Microns per Second, Volts per Cm.)	Average Reduction of Mobility (Expressed in per Cent Under Mobility in the Salt Solution Control)								
			Rabbit Serum (1:800)		Horse Serum (1:800)		Human Serum† (1:320)				
			No. 185* Immune	Normal	Immune	Normal	Pemphigus (Patient 75)	Lupus Erythematosus (Patient 77)	Dermatitis Herpetiformis (Patient 83)	Erythema Multiforme (Patient 66)	Normal
Pemphigus	18	2.58	61	16	50	15	65	34	30	33	5
Lupus erythematosus	7	1.61	17	+3	+15	+9	+2	45	+2	4	+13
Dermatitis herpetiformis	4	2.19	28	28	16	22	20	27	60	25	17
Erythema multiforme	4	1.95	0	0	0	0	14	16	16	51	6
Encephalitis	6	1.99	20	8	10	6	14	16	16	12	8
Arthritis	6	2.02	14	+7	+9	+7	+1	1	3	5	+5

* The serums of twelve other rabbits immunized with single strains of the streptococcus from patients with pemphigus gave similar results.

† The serums from three patients with each of the four diseases named in this part of the table (twelve serums in all) gave similar results.

TABLE 6.—*Removal from Immune Rabbit and Horse Serums of the Mobility-Reducing Action by Absorption with Heterologous Strains of the Streptococcus*

Source of Streptococci	Average Mobility in Salt Solution (Microns per Second, Volts per Cm.)	Serums from Animals Immunized with the Streptococcus from Patients Who Had Pemphigus					
		Rabbits (Pool of 13; 1:320)			Horse (1:320)		
		Nonabsorbed, per Cent	Treated with Streptococci from		Nonabsorbed, per Cent	Treated with Streptococci from	
			Pemphigus, Strain 18, per Cent	Arthritis, Six Strains, per Cent		Pemphigus, Strain 17, per Cent	Arthritis, Six Strains, per Cent
Pemphigus, pool of nineteen strains	2.16	52	10	51	48	19	48
Pemphigus, strain 1	2.19	48	13	47	51	18	54
Pemphigus, strain 3	3.34	74	46	73	49	19	50
Pemphigus, strain 5	2.24	49	19	47	44	21	49
Pemphigus, strain 9	1.96	49	7	58	40	1	37
Dermatitis herpetiformis, strain 1	2.17	17	14	17	14	20	19
Lupus erythematosus, strain 2	1.71	6	5	5	+8	+6	+5

MOBILITY IN SERUM FROM WHICH IMMUNE BODIES HAD BEEN ABSORBED

It was then demonstrated that the mobility-reducing action of the immune horse serum and pooled immune rabbit serum could be removed by absorption of the immune bodies with heterologous strains of the same streptococcus from pemphigus.

In table 6 it is evident that the pooled immune rabbit serum from which antibodies had been absorbed by a single strain (18) and the immune horse serum from which antibodies had been absorbed by a single strain (17) of the streptococcus isolated from patients with pemphigus reduced the mobility, compared with the average mobility in a sodium chloride solution, of a pool of nineteen strains and four single strains of streptococci from the same source only a small percentage compared with the great amounts in which the mobility of the same streptococci was reduced by the same serums with agglutinins unabsorbed. The pooled immune rabbit serum and the immune horse serum treated with a pool of six strains from patients who had arthritis behaved practically as did these serums untreated.

The reduction of the average mobility of control streptococci isolated from patients who had lupus erythematosus and dermatitis herpetiformis was slight and practically the same whether the serums were treated or untreated.

Similar results were obtained in further experiments of which those recorded in table 6 are examples; as many as eighteen different test strains of the organism from patients with pemphigus were used, and the immune serums were treated with strains other than numbers 17 and 18, which had been isolated from patients who had pemphigus.

The mobility-reducing action on the respective streptococci of the serums from patients who had pemphigus, lupus erythematosus and dermatitis herpetiformis was removed by treating these serums with the respective heterologous strains of streptococci. Table 7 records this phenomenon for the serum from a patient for each of the diseases named.

It can readily be seen that each serum, when treated with heterologous strains of the respective streptococci, reduced the mobility of the control and the respective streptococci about equally. Each of these serums untreated and each serum treated with control streptococci markedly reduced the mobility of the respective streptococci and not that of the controls.

THE DIAGNOSTIC TEST

The mobility-reducing action of the serums from patients with pemphigus, dermatitis herpetiformis, lupus erythematosus and erythema multiforme on the respective streptococci, as shown by comparison with

the mobility in sodium chloride solution was found to be so specific in experiments such as those just described that an attempt was made to apply this action as a differential diagnostic test for these four diseases.

Table 8 demonstrates the results of a typical positive test with the serum from a patient for each of the diseases named. It is to be noted that each serum reduces markedly the mobility of the pool of strains of streptococci from patients with the respective disease, whereas it reduces

TABLE 7.—*Removal from Immune Human Serums of the Mobility-Reducing Action by Absorption with the Respective Heterologous Strains of Streptococci*

Source of Streptococci	Average Mobility in Sodium Chloride Solution (Microns per Second, Volts per Cm.)	Serums from Patients Who Had: Pemphigus; Treated with Streptococci from: Nonabsorbed, per Cent	Pemphigus, Strain 5, per Cent	Dermatitis Herpetiformis, Strain 105, per Cent	Lupus Erythematosus; Treated with Streptococci from: Nonabsorbed, per Cent	Lupus Erythematosus, Strain 1, per Cent	Arthritis, Six Strains, per Cent	Dermatitis Herpetiformis; Treated with Streptococci from: Nonabsorbed, per Cent	Dermatitis Herpetiformis, Strain 1, per Cent	Pemphigus, Pool of Nineteen Strains, per Cent
Pemphigus, strain 1	2.65	..	..	..	..	..	..	26	28	31
Pemphigus, strain 3	3.34	74	29	64						
Pemphigus, strain 4	1.84	55	+15	35						
Pemphigus, strain 12	2.46	73	11	57	31	31	30			
Lupus erythematosus, strain 2	1.92	21	3	16	57	22	49	16	19	15
Lupus erythematosus, strain 3	1.73	..	..	..	60	25	53			
Lupus erythematosus, strain 4	1.41	..	..	..	46	+4	49			
Dermatitis herpetiformis, strain 1	2.17	18	20	24	28	21	22	59	16	49
Dermatitis herpetiformis, strain 2	2.20	..	..	..	..	..	..	60	12	53

Similar tests with other serums from patients with the diseases named here, treated with still other strains of the respective streptococci, gave results similar to those represented in this table (serum dilution, 1:320).

the mobility of the streptococci from patients with the other three diseases little or no more than does normal serum. The average mobility of the streptococci in the pools varies from day to day. Normal serum reduces slightly the mobility of all of the streptococci. This test was applied to serums from several patients in the case of each of the four diseases, and in every instance only the mobility of the respective streptococci was reduced appreciably.

Several colleagues in dermatology in neighboring cities collaborated by sending me blood from patients with these four diseases.

To date, positive tests for pemphigus have been obtained with serums from fourteen patients, in twelve of whom the condition was diagnosed as pemphigus and in one of whom it was diagnosed as erythema multi-

forme. A positive test for pemphigus was obtained with the serum of a patient in whose case a definite diagnosis has not yet been made. The differential diagnosis in this case rests between pemphigus foliaceus and pityriasis rubra pilaris. Positive tests for dermatitis herpetiformis were obtained with serums from fifteen patients, in eleven of whom the condition was diagnosed as dermatitis herpetiformis and in four of whom

TABLE 8.—*Diagnostic Test. Application, as a Diagnostic Test, of the Mobility-Reducing Action (Expressed in Per Cent Under the Average Mobility in Salt Solution) of the Serums from Patients with Pemphigus, Dermatitis Herpetiformis, Lupus Erythematosus and Erythema Multiforme, on the Respective Streptococci*

Typical Positive Test for	(Serum Dilution 1:640) Source of Serum	Antigens: Pooled Strains of Streptococci from			
		Pemphigus (Case 102)	Dermatitis Herpetiformis (Case 103)	Lupus Erythematosus (Case 104)	Erythema Multiforme (Case 132)
Pemphigus	Pemphigus (case 142).....	60%	28%	27%	7%
	Normal.....	23%	22%	20%	7%
	Mobility in salt solution (control).	1.95*	1.85	1.79	1.24
Dermatitis herpetiformis	Dermatitis herpetiformis (case 21)....	21%	40%	+4%	3%
	Normal.....	24%	+7%	5%	3%
	Mobility in salt solution (control).	2.02	1.38	1.41	1.50
Lupus erythematosus	Lupus erythematosus (case 110).....	12%	+4%	60%	8%
	Normal.....	6%	6%	6%	7%
	Mobility in salt solution (control).	1.89	1.40	1.39	1.30
Erythema multiforme	Erythema multiforme (case 121)...	12%	12%	8%	60%
	Normal.....	19%	15%	15%	8%
	Mobility in salt solution (control).	2.10	2.04	2.01	1.91

* Microns per second, volts per centimeter.

it was diagnosed as pemphigus. Positive tests for lupus erythematosus were obtained with serums from seven patients, in five of whom the condition was diagnosed as lupus erythematosus and in two of whom it was diagnosed as the Senear-Usher syndrome. Positive tests were obtained for erythema multiforme with serums from eight patients, in six of whom the condition was diagnosed as erythema multiforme and in two of whom it was diagnosed as pemphigus.

Thirty-two control serums have been tested; they comprised seven from normal persons, two from patients with acne rosacea, one from a patient with pyodermia gangraenosa, one from a patient with

hemorrhagic bullous trichophytid, eight from patients with herpes zoster, four from patients with varicella, one from a patient with bullous impetigo, four from patients with lichen planus, two from patients with pityriasis rosea and two from patients with herpes gestationis. All failed to reduce appreciably the cataphoretic mobility of the pooled streptococci from patients with pemphigus, dermatitis herpetiformis, lupus erythematosus and erythema multiforme.

All of the results obtained by injection into animals, by injection into patients with pemphigus, by serologic studies and by determinations of the mobility of the streptococcus in immune serum were obtained with the streptococcus after it had been rapidly subcultured as many as seventeen times in dextrose-brain broth.

SUMMARY

A streptococcus having specific morphologic, cultural and fermentation characteristics and a characteristic cataphoretic mobility distribution curve has been isolated from patients with pemphigus. It has been found to be virulent for five species of animals and to produce lesions consistent with pemphigus in a fair number. Intradermal and subcutaneous injections of the dead organism into patients with pemphigus produce bullae. The different strains have been shown to be serologically identical. Positive precipitin reactions between the nasopharyngeal washings from patients with pemphigus and the serums of animals immunized to the specific streptococcus are described. The reduction of the mobility of the respective streptococci by the serums from patients with pemphigus, dermatitis herpetiformis, lupus erythematosus and erythema multiforme, as compared with their mobility in a solution of sodium chloride, is applied as a differential diagnostic test between these four diseases.

ABSTRACT OF DISCUSSION

DR. L. A. BRUNSTING, Rochester, Minn.: The discussion of this paper should be the function of a bacteriologist, and I regret that Dr. Rosenow is unable to be here. It is rather unusual to find an expert bacteriologist and a dermatologist combined in the same person. Dr. Welsh has done every bit of this work, from the isolation of the streptococcus to its inoculation into animals, and most of the work has been done in the small hours of the morning; his studies have included many thousands of observations by the Northrop-Kunitz-Mudd cataphoresis apparatus, the observation of which is a tedious procedure. He did not emphasize enough that those who attempt to confirm his work should be sure that they are dealing with freshly isolated organisms, and that the technic is being closely followed. It seems to me significant that the organisms have been isolated from the circulating blood on ten occasions in five of these patients.

Investigators are a long way from deciding the specificity of an organism from cultural and morphologic characteristics. It is possible that previous reports dealing with organisms isolated in pemphigus have been concerned with one or the

other of these pleomorphic strains which Dr. Welsh has discussed. The fact that man has a relatively low antigenic titer for streptococci has led Dr. Welsh to produce the immunologically higher titer in animals in order to demonstrate the phenomena of specific precipitation, agglutination and absorption.

His experiments have been adequately controlled, not only as regards normal persons, but likewise as regards patients with many of the other bullous dermatoses, particularly varicella, herpes zoster, erythema multiforme, disseminated lupus erythematosus and dermatitis herpetiformis.

Estimation of cataphoretic mobility by this apparatus was first brought out for the study of colloidal particles in chemistry, and it has been adapted to bacteriology. These organisms proceed in the microscopic field toward the positive pole, with a mobility proportional to the negative charge which each organism contains, and it is startling to see the specific inhibitory effect of certain serums on particular streptococci.

The method is a decided advance and an addition to the contributions of Pels and Macht in regard to the differential diagnosis of pemphigus. Serum from a patient suspected to have pemphigus can be sent from a distance to be studied in this way against pooled organisms which have been isolated from patients known to have pemphigus.

Dr. Welsh is carrying his work further by building up immunologic serums which can be used for passive desensitization of such patients.

Dr. Theodore Cornbleet, Chicago: Dr. Welsh's work is impressive because of the immense amount of work entailed and because it is so well thought out.

Without corroboration the specificity of the organism is still questionable, but I think that Dr. Welsh has succeeded in showing that the blood of the patient with pemphigus has specific properties; this is a continuation, of course, of the work of Pels and Macht.

Some time ago I reported studies on the differences in capillary permeability between patients with pemphigus and patients with other bullous eruptions and particularly those with dermatitis herpetiformis. I found in those experiments that the permeability of patients with pemphigus was much greater than that of patients with dermatitis herpetiformis, and my associates and I proposed a differential test on that basis. The test is based on the ability of protein to leave the blood vessels and enter the blister fluid or the blister. The determination of the ease with which a protein molecule leaves the blood vessel and enters the blister depends on the surface charge, among other things, and that, of course, is given it by the blood that bathes the molecule. In the same way, any other body that lies immersed in this pool of blood will be given similar charges. I think that what Dr. Welsh has done by his cataphoretic experiments is to measure in units this particular property which blood from patients with pemphigus has, and which is transmitted to bodies immersed in it. I think that what has been done is not so much the isolation of any specific organism as the definition of the properties of the blood in pemphigus.

Dr. A. L. Welsh, Rochester, Minn.: The determination of streptococcus mobility in serum is a technical procedure, and I could not hope in the short time given here to go into any great detail as to its nature; in the paper I have made it somewhat clearer.

I have received two serums from patients whose condition was clinically diagnosed as the Senear-Usher syndrome. It was interesting to note that when these serums were tested by this method they gave no reaction with the antigen of pemphigus but gave strongly positive reactions with that of lupus erythematosus.

MUCHA-HABERMANN SYNDROME (PARAPSORIASIS VARIOLIFORMIS)

A CRITICAL STUDY WITH A REPORT OF A CASE

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LOS ANGELES

One of the most interesting cutaneous syndromes recently discussed in dermatologic literature is the condition described by Mucha,[1] in 1916, and then by Habermann,[2] in 1921, under the name of pityriasis lichenoides varioliformis acuta. Cases of the Mucha-Habermann syndrome are sufficiently rare to be recorded. Forty-three are reported in the literature. The number of actual cases must be much larger, but most of them are undoubtedly not recognized because the morphologic and clinical picture of the Mucha-Habermann syndrome is still unfamiliar to the rank and file of dermatologists and the medical profession.

What makes the cases of Mucha-Habermann syndrome still more interesting is the uncertainty of the nosologic classification and the sharp differences of opinion voiced in the literature in this regard.

For these reasons I am reporting a case and shall review the literature.

REPORT OF A CASE

History.—M. R., a man, aged 34, was first seen on Oct. 18, 1932, complaining of a cutaneous eruption. His father died at the age of 56 of tumor of the bladder. The mother, living, aged 65, was suffering from "heart trouble and goiter." The patient had no knowledge of other diseases in the family, and specifically denied having had syphilis or tuberculosis. He had chickenpox, measles, mumps and whooping cough in childhood and a sore throat when 18 years old. His tonsils were removed in 1917. He was vaccinated successfully against variola at the age of 15 and was revaccinated at 18 years of age. He received triple typhoid vaccination in the army in 1918. His hair had always been thin, and started to fall out at about the age of 20. Slight acne, noted at intervals, had never been severe. In 1925 he was working in a rubber factory and was exposed to the fumes of sulphur bisulphide, carbon tetrachloride and benzene. He had a protracted cold, which cleared up when he quit that work on the advice of a physician. He had been doing clerical work since, and at the time of examination was employed as a bookkeeper. Occasionally he was slightly constipated, for which he took proprietary effervescent saline laxative. He denied having a venereal disease or exposure.

About Sept. 1, 1932, when removing his stocking, the patient noticed that a scab came off the right ankle, leaving a moist reddened area which healed slowly,

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1. Mucha: Arch. f. Dermat. u. Syph. **123**:586, 1916.
2. Habermann: Dermat. Ztschr. **45**:42, 1926.

leaving a purplish, thin scar. There was no pain or itching. About three weeks later he noted a number of small lesions on the outer aspect of the left arm, several of which broke down and became sore. About the same time he noted a few similar areas on the abdomen, not itching or painful, but small, brown, smooth patches. On October 18, about six weeks after the appearance of the first lesion he was referred to me by Dr. Emerson Savage. A diagnosis of parapsoriasis varioliformis was made. The patient was presented before a meeting of the dermatologic section of the Los Angeles County Medical Association on November 13, at which time the diagnosis was generally concurred with.

The lesions continued to increase, appearing singly or in crops and gradually becoming papular, when the skin over them would break down or scale off and the lesions would gradually involute, leaving brown scars. About November 1, a

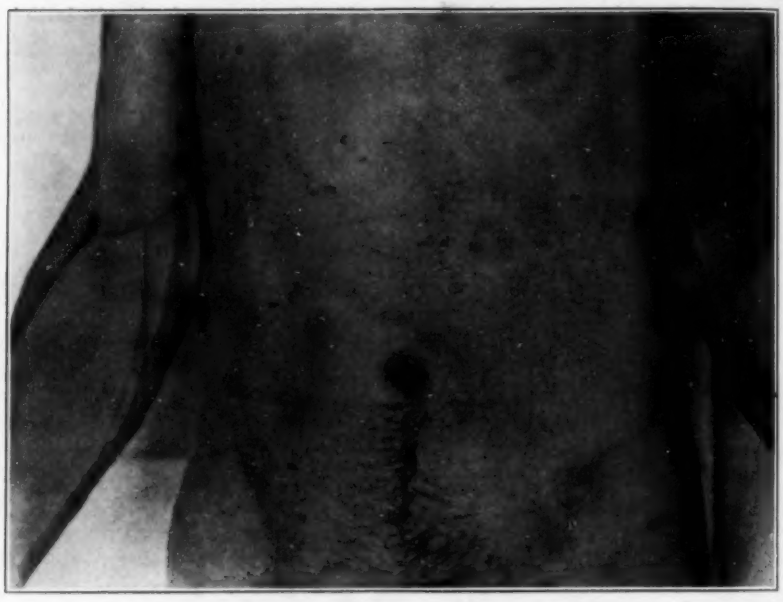

Fig. 1.—Mucha-Habermann syndrome.

large number of the lesions appeared over the hips, thighs and waist and over the outer aspects of both arms.

Physical Examination.—The patient was a white man, of medium height (67¾ inches [172 cm.]), slight, weighing 142 pounds (64.4 Kg.), thin but fairly well nourished and not apparently ill. His complexion was fair. The teeth were in good condition, the lips thin, the tonsils absent and the throat clear. None of the superficial glands throughout the body (cervical, axillary, epitrochlear, inguinal and popliteal) were enlarged. Examination of the chest revealed no abnormal or adventitious sounds. The heart sounds were regular, the pulse rate was 76, and the blood pressure 125 systolic and 80 diastolic. The peripheral vessels did not show arteriosclerosis. The abdomen was flat. The spleen and the margin of the liver could not be felt. There were no abnormal masses or tenderness. No varicose veins were seen.

Laboratory Examination.—The urine was clear and light in color, having a specific gravity of 1.02. There was no evidence of sugar, albumin, abnormal cells or indican, and no diazo-reaction was obtained. The blood showed: hemoglobin content, 75 per cent (Dare); red blood cells, 5,080,000; white blood cells, 9,500; polymorphonuclears, 70 per cent; lymphocytes, 25 per cent; eosinophils, 2 per cent, and monocytes, 3 per cent. Sedimentation time was three hundred minutes (Linzenmeier), normal at 74 mg. per hundred cubic centimeters. The Wassermann reaction (Kolmer) was negative; the Kahn test (standard and presumptive),

Fig. 2.—Mucha-Habermann syndrome.

negative. A roentgenogram of the chest showed the lungs well aerated. There was no evidence of tuberculosis.

Cutaneous Examination.—Examination revealed a polymorphous eruption involving mainly the trunk and limbs. The face, hands, feet and genitals were free from lesions. Speaking generally, the distribution suggested strongly that of pityriasis rosea. The eruption consisted of several types of lesions, sharply defined and discrete, without the slightest tendency to coalescence or fusion. The number of lesions probably reached several hundred, but an exact count was hardly possible as they constantly involuted and sprang up in new crops.

The most prevalent type were dry macules and papules, round or oval, varying in size from that of a linseed to that of a small coffee-bean. The lesions were yellowish red, a few deep red, slightly elevated and covered with fairly adherent scales. A few of the papular lesions were denuded of these scales, and presented deep red waxy bases. There were several dozen oblong and irregularly shaped lesions covered with hemorrhagic and blackish necrotic crusts.

There were also a score of erosive lesions, apparently the result of the involution and healing of the necrotic crusted lesions. Some of these erosive lesions reached a depth of 2.2 mm., and could be called ulcerations. The base of the ulcerative lesions presented a fairly dry, deep red, healthy granulating surface. On healing they formed soft varioliform scars. There were six scars of this type scattered over the trunk and limbs. The largest ulcerated lesions were symmetrically located on the inner sides of the thighs, and two others were also symmetrically situated at the outer end of Poupart's ligament. The bulk of the eruption was on the trunk. The upper limbs showed ten big lesions and a number of small ones. The legs showed a number of small papular lesions. The right ankle showed a large scar, the site of the first lesion, which was followed two weeks later by the patches on the chest. There were no frank vesicles, but many of the crusted hemorrhagic lesions suggested development from a vesicle. On November 8, a specimen was taken for biopsy from two lesions near the elbow on the left arm, one an early lesion that had just begun to appear papular and elevated and the other an older lesion that showed beginning vesiculation and central necrosis.

Histopathologic Observations (Dr. Emil Bogen).—The section of an early lesion, taken from the left arm near the elbow, was fixed in a solution of formaldehyde, embedded in paraffin, cut and stained with hematoxylin and eosin. The stratum corneum was not specially thickened in any part, but was separated from the remainder of the section just over the lesion by clear empty spaces which probably had contained some fluid. There were two small areas of the stratum corneum in which nuclei might be seen in deeper staining keratinized material, but most of the horny layer did not show this appearance of parakeratosis.

The stratum granulosum was less deeply stained and discrete over the center of the lesion than in the more normal skin, and did not appear to be thickened.

The cells of the rete Malpighii appeared slightly edematous, somewhat paler than in the normal areas, and did not seem to have differentiated as readily as usual in passing from the basal to the granular layer. There was some increase in the thickness of the spinous layer, but no notable proliferation of daughter processes or extension of the basal layer in the interpapillary regions. There were clear spaces, usually globular and mostly small but abundant, in the rete and also in the basal and papillary layers, which suggested the shrinkage of edematous cells in this layer under the processes of fixation, but which possibly existed before the fluid spaces. The nucleoli in the rete cells appeared more prominent than normally, while others were pyknotic and shrunken.

The basal layer was somewhat disorganized, the orientation in some places was lacking, and the continuity of the basal membrane was interfered with by small clear spaces or by infiltration by small round cells and narrow connective tissue cells. The papillary layer of the corium was somewhat darker than the deeper portions of the corium, owing mainly to the presence of an increased number of connective tissue nuclei in this region and also a few leukocytes. Here also was evidence of intercellular edema in the form of clear narrow spaces.

There was marked hyperemia with enlargement of the blood vessels, specially marked in the deeper layers of the corium. The vessels were surrounded by narrow zones of dense perivascular cellular infiltration consisting mainly of small round cells and thin dense connective tissue cells. A few plasma cells were present.

In general the lesion was of an inflammatory character with edema in nearly all the layers of the skin, but with the cellular infiltrate limited to narrow perivascular zones, marked hyperemia and beginning fibroblastic stimulation. A section of the more advanced lesion was similarly prepared. The stratum corneum was thin,

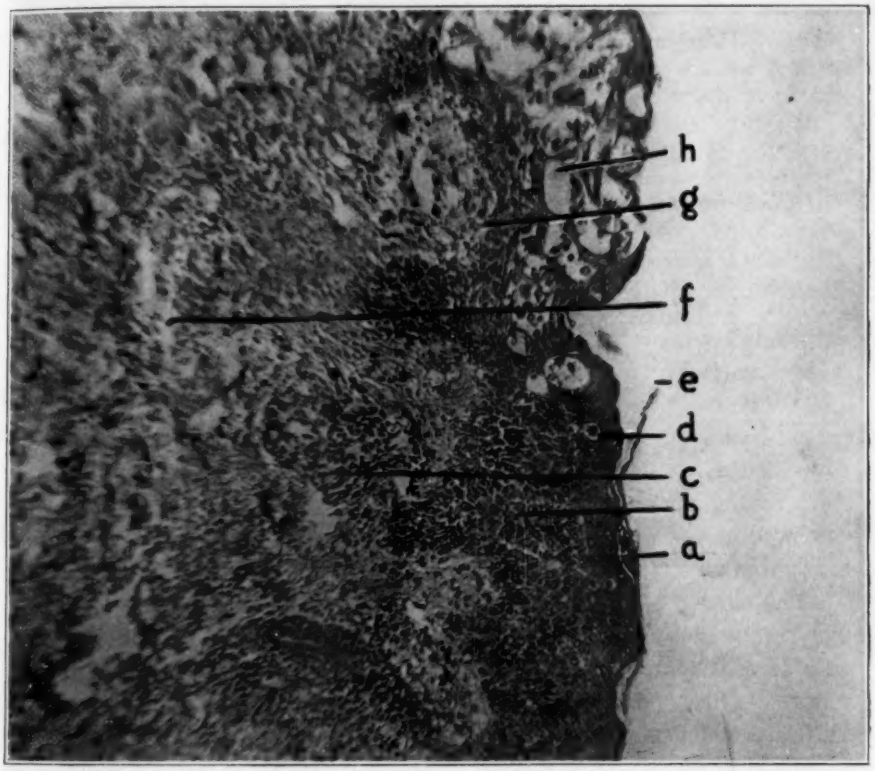

Fig. 3.—Photomicrograph of the early lesion (high power): *a*, parakeratosis; *b*, swollen rete cells; *c*, subcuticular round cell infiltrate; *d*, balloon degeneration in the rete; *e*, desquamating scale; *f*, edema in the subpapillary layer; *g*, disorganization of the basal layer, and *h*, a microscopic vesicle.

contained numerous nuclear remains (parakeratosis) and was stained more deeply than the normal areas. It was separated from the rete by a network of fibrinous material with large fluid spaces containing many small round cells. These small round cells were found in and on the stratum corneum as well as in the deeper layers. The stratum granulosum was practically absent.

The rete Malpighii was markedly edematous, containing numerous clear open spaces, an infiltration of small round cells and occasional slender fibroblasts. The cells appeared swollen and pale and showed a subnormal amount of differentiation.

The basal layer was disorganized, being discontinuous in many areas, with the basal membrane absent and the epithelial cells in places surrounded by the connective tissue fibers of the corium. Marked edema and fluid spaces were seen. Many of the epithelial cells were indistinct and blurred and showed signs of disintegration. The papillary layer of the corium in places blended imperceptibly with the epidermis, containing numerous small round cells and connective tissue nuclei.

The subpapillary layer showed edema, hyperemia and more intense perivascular infiltration than in the earlier section. There were more leukocytes and plasma cells and many epithelioid cells in the infiltrate, the small round cells and the large clear epithelioid cells and slender deep-staining connective tissue cells, however, being the predominating types.

Course.—The course was surprisingly smooth and uneventful for a dermatosis which at the first glance gave the impression of a deep systemic if not a serious condition. Under simple treatment with 2 per cent ammoniated mercury ointment, systemic ultraviolet irradiation and a tonic mixture containing iron and arsenic the lesions began slowly to improve. New lesions, individually or in small crops, appeared now and then, but the condition in general cleared up steadily until, after five months, the patient was completely free from lesions.

MORPHOLOGY

The intricacies and elusiveness of morphologic classification have not been demonstrated as strikingly in any other group of dermatoses as in parapsoriasis. Since Brocq synthesized the concept of parapsoriasis and suggested three types of parapsoriasis, guttata, lichenoides and in plaques, many observers have reported a large number of cases and have suggested a bewildering array of descriptive names for the condition. As a result, not only the beginner, but also the specialist is baffled and confused in visualizing and differentiating the various forms. It seems to me that Brocq's classification is the simplest and most logical.

The climax of the confusion and conflicts of morphologic concepts was reached when Mucha [1] of Vienna reported what he thought to be a case of anomalous parapsoriasis. Several observers have made similar reports. One, Habermann,[2] suggested the name of pityriasis lichenoides varioliformis acuta, which has been generally adopted. Fred Wise [3] somewhat improved it by calling it parapsoriasis varioliformis acuta.

If one compares the morphologic picture and clinical behavior of the newly suggested form of parapsoriasis with the hitherto accepted chronic form, as it has been aptly termed by Walter Highman,[4] one is likely to be struck not by similar morphologic and clinical features, but by differences so fundamental and so in conflict with the established concept of parapsoriasis as to make one feel justified in questioning seriously the advisability of placing the new syndrome in the group of parapsoriasis.

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3. Wise, Fred: Parapsoriasis, New York State J. Med. **28**:901 (Aug.) 1928.

4. Highman: Value of the Study of Histopathology in Cutaneous Medicine, J. A. M. A. **87**:1459 (Oct. 30) 1926.

One common morphologic feature of these conditions is the oval and round macular and papular lesions. Granting even that individual papules and macules bear a certain resemblance to those of parapsoriasis, the lesions by themselves are not pathognomonic morphologically, but occur in other psoriasiform dermatoses. The scales of many of the papular lesions in my case were not thin and filmy, but were much heavier, of a type not seen commonly in parapsoriasis, being more superficial and greasy and approaching the seborrheic or mycotic form. Leaving this feature of papular and macular lesions, the rest of the morphologic picture and clinical behavior are sharply at variance with the accepted type of parapsoriasis, and flatly contradict its clinical features.

To start with, parapsoriasis was conceived as an eruption consisting of dry, slightly infiltrated papules and patches. Vesicles and hemorrhagic and necrotic lesions were practically never observed in the accepted cases of parapsoriasis. The reports of such exceptional observations among many thousand cases are so few as to justify failure to consider them as conclusive clinical evidence, for they might have represented a mere accidental coexistence of the nosologic entities. Parapsoriasis was conceived as preeminently chronic, practically stationary and resistant to all types of treatment. The newly suggested form is acute or subacute, apparently is self-limited and clears up practically without treatment.

The accepted morphologic concept of parapsoriasis presents only one type of lesion, papules and macules, though it may present innumerable variations of pattern or figures of the eruption, such as striped, retiform, guttate, diffuse, generalized, irregularly shaped, mixed or freakish.

The new variety, on the contrary, is distinctly polymorphous, presenting macular, papular, vesicular, hemorrhagic, necrotic, ulcerative and scarry lesions. On the other hand, its pattern, judging from the descriptions and illustrations of the reported cases, is remarkably uniform. It mimics and suggests strongly the pattern of pityriasis rosea extending beyond its regular boundaries. In all varieties of lesions of parapsoriasis, while some may remain discrete, many others have a tendency to become vague and diffuse in outline and to coalesce in patches or large areas. In the new Mucha-Habermann syndrome lesions are sharply defined and discrete, and continue thus throughout the course of the disease.

Furthermore, the course of parapsoriasis is notoriously slow, insidious, progressive and stationary after it reaches the acme of its development. Recurrences are unknown. The new variation, on the contrary, shows consistently a fairly acute onset and development and involution of the lesions in crops. Finally, the new variety shows a marked predominance of cases in the male sex while parapsoriasis does not show a preference in sex.

Differential Characteristics.—The following list illustrates in a graphic way the marked morphologic and clinical difference between parapsoriasis and the Mucha-Habermann syndrome:

PARAPSORIASIS	MUCHA-HABERMANN SYNDROME
1. Distinctly chronic	1. Acute and subacute
2. Persistent indefinite course	2. Self-limited (a few weeks or months)
3. Insidious, progressive or stationary	3. Lesions develop in crops
4. No preferences to sex	4. Attacks mostly males
5. Resistant to any treatment	5. Responds to any treatment
6. One type of lesion only: maculopapular	6. Distinctly polymorphous maculopapular, vesicular, hemorrhagic necrotic; scars
7. Sharply defined and diffuse lesions, discrete and coalescing into patches	7. Always sharply defined; discrete throughout course
8. Generally attacks trunk and limbs, but often unilateral; seldom symmetrical	8. Uniformly bilateral, often symmetrical, suggesting pityriasis rosea
9. No subjective or systemic symptoms	9. At times itching; systemic symptoms in a few cases
10. Scales faint, filmlike, firmly adherent and waxy	10. In my case heavier, superficial, greasier scales suggesting seborheic or mycotic condition
11. Pattern and figure of eruption presents endless variations—guttate, diffuse, irregular, freakish, mixed striped, reticular	11. Remarkably uniform, suggesting pityriasis rosea

With so many morphologic and clinical differences between the Mucha-Habermann syndrome and parapsoriasis it is small wonder that opposition has developed to the theory of identity of the conditions. In Europe, Bushke,[5] Riel, Kyrle and Oppenheim[6] regard the new syndrome as a separate entity. In this country Pusey, Pollitzer, Highman,[4] Satenstein, Michelson and Diasio[7] also oppose the acceptance of the identity of the two conditions. On the other hand, Fred Wise,[8] Senear and Oliver,[8] Gross[9] and Crawford[10] are inclined to accept the Mucha-Habermann syndrome as a variety of parapsoriasis.

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5. Bushke, in discussion of Bruhns: Zentralbl. f. Haut- u. Geschlechtskr. **24**: 322, 1927.

6. Oppenheim: Wien. dermat. Gesellsch. **10**:6, 1919; Arch. f. Dermat. u. Syph. **133**:119, 1921; Zentralbl. f. Haut- u. Geschlechtskr. **1**:107 and 217, 1921.

7. Diasio, F. A.: Pityriasis Lichenoides et Varioliformis (Habermann), Arch. Dermat. & Syph. **24**:72 (July) 1931.

8. Senear, F. E., and Oliver, E. A.: Pityriasis Lichenoides et Varioliformis Acuta (Habermann), Arch. Dermat. & Syph. **23**:12 (Jan.) 1931.

9. Gross, P.: Pityriasis Lichenoides et Varioliformis Acuta, Arch. Dermat. & Syph. **23**:33 (Jan.) 1931.

10. Crawford, S.: Pityriasis Lichenoides et Varioliformis Acuta, Arch. Dermat. & Syph. **26**:990 (Dec.) 1932.

HISTOPATHOLOGY

Those who believe in the identity of the two conditions are well aware of, and admit, the considerable morphologic differences between the Mucha-Habermann syndrome and parapsoriasis. Therefore, they do not dwell on the morphologic differences, but stress as their major argument the histopathologic resemblance of the two conditions. Their arguments are tenable only on the assumption that the histopathologic picture of parapsoriasis is so characteristic that its diagnosis can be made on microscopic observations alone, irrespective of the morphologic and clinical data.

The fact is, however, that the histopathologic picture of parapsoriasis is far from being definite and clearcut, much less pathognomonic. Histopathologists regard the picture as suggestive, but not as absolutely characteristic, and they disagree on many important details. Thus, Pollitzer, one of those who originally described pityriasis lichenoides with Unna, in 1890, said: "There is no more difficult microscopic picture than parapsoriasis. I would never make a diagnosis of parapsoriasis on a histopathologic report." Walter Highman said, "Parapsoriasis can only be surmised on a histologic picture, but not established without clinical data. Despite the distinctiveness of the disease the histopathologic changes are astonishingly slight." McCarthy,[11] in his manual on the histopathology of cutaneous diseases, basing his conclusions on the collective opinion of the recognized authorities on the histopathology of the skin said that "the lack of a characteristic and typical histopathologic picture in parapsoriasis serves to distinguish it from lichen planus, syphilis and psoriasis." Arndt pointed out that a diagnosis of parapsoriasis based on microscopic observations alone is uncertain and is justified only when clinical and histologic data are correlated. Satenstein never saw vesicular or necrotic lesions in parapsoriasis. On both a pathologic and a clinical basis he rejected the identity of the Mucha-Habermann syndrome with parapsoriasis and considered it a separate entity.

In the face of these authoritative citations it is hard to see how one can base a conclusion as to the identity of the Mucha-Habermann syndrome with parapsoriasis on the debatable and uncertain fact of histopathologic resemblance when there is such overwhelming clinical evidence to the contrary. It is of interest that most of the histologic reports submitted in support of identity are fragmentary and bring out various histopathologic features of diverse diagnostic value. Practically none of them tabulate in detail the morphologic differences and resemblances of the dermatoses under discussion or emphasize their relative importance in differential diagnosis.

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11. McCarthy, L.: Histopathology of Skin Diseases, St. Louis, C. V. Mosby Company, 1931.

Table 1, compiled from the data of McCarthy,[11] graphically presents the histopathologic details of dermatoses having some clinical resemblances and entering the differentiation between the Mucha-Habermann syndrome and parapsoriasis.

It is of interest that Mucha and Habermann, by whose name the syndrome is designated, were in disagreement as to various histopathologic details. Habermann accepted Mucha's histologic observa-

TABLE 1.—*Comparative Histopathologic Changes of Parapsoriasis Varioliformis*

	Parapsoriasis Varioliformis	Parapsoriasis Lichenoides	Parapsoriasis Guttata	Psoriasis	Pityriasis Rosea	Secondary Syphilid	Tuberculid	Varicella	Variola	Lichen planus
Horny layer										
Hyperkeratosis	−	−	+	+	..	−	−	−	−	+
Parakeratosis	++	++	+	++	+	−	−	−	−	−
Serous exudative and fibrinous crust	+−	−	−	−	++	−	++	−	−	−
Cellular exudate	−	−	..	−	−	−	++	−	−	−
Granular layer										
Absent	++	−	+	+	+	−	−	+	+	−
Increased	−	−	−	−	−	−	−	−	−	++
Rete										
Acanthosis	+	++	−	+	++	+	+−	−	−	++
Spongiosis	+	++	−	+	+	−	−	−	−	−
Edema	+−	+	+	+	+	−	−	+	+	−
Degeneration	++	++	+	+	−	−	−	+	+	−
Necrosis	++	−	−	−	−	−	−	−	−	−
Fluid:										
Multilocular	++	−	−	−	+	−	−	+	−	−
Unilocular	−	−	−	−	−	−	−	−	+	−
Infiltration of lymph	+	+	−	+	+	++	++	+	+	+
Leukocytes	−	−	+	−	−	−	−	+	+	..
Basal layer										
Intact	−	−	−	+	+	+	+	−	+	−
Disoriented	+	+	+	−	−	−	−	+	−	+
Edematous	+	+	+	+	+	−	−	+	−	−
Infiltrated	+	+	+	−	+	++	++	+	+	+
Papillary layer										
Edema	+	+	+	+	++	..	−	+	+	−
Infiltrate	+	+	+	+	++	+++	+	+	+	++
Subpapillary layer										
Edema	+	+	+	+	−	−	−	+	+	−
Infiltrate	+	+	+	+	+	++	+++	+	+	−
Congestion	+	+	+	+	−	+	−	+	+	−
Blood vessels dilated	+−	+	+	+	+	++	−	+	+	+
Follicles infiltrated	+−	++	+	+	+	−	−	−	−	−
Glands infiltrated	+−	+	+	+	+	−	−	−	−	−

tions of the marked destruction of epidermis and thick infiltrate of the upper cutis. Yet he disagreed with Mucha in accepting these changes recognized by all observers as characteristic of parapsoriasis. Habermann cited Ricke, who found besides hyperkeratosis and parakeratosis only moderate infiltration of the papillary body and epidermal layers.

Most reporters failed to observe that three varieties of parapsoriasis differ slightly in histopathologic details, which can be seen from McCarthy's citations. On the other hand, Highman stated: "Despite the wide variations in gross appearances of the lesions, the microscopic pictures of the lesions of all types of parapsoriasis are singularly uniform,

and despite the distinctiveness and chronicity of the disease the histologic changes are astonishingly slight."

Most observers reporting cases of the Mucha-Habermann syndrome did not discuss the question of the identity of or differences in the three recognized varieties of parapsoriasis. Apparently all of them compared the acute conditions with parapsoriasis guttata and parapsoriasis (pityriasis) lichenoides, two conditions which are seemingly regarded as closely similar if not identical. Because of the greater clinical differences few observers mention parapsoriasis in plaques.

One histopathologic feature mentioned consistently by all reporters of the Mucha-Habermann syndrome is a disorganization of the basal layer of the rete. However, even this feature is not pathognomonic

TABLE 2.—*Histopathologic Changes of American Observers*

	Wise[5]	Senear and Oliver[6]	Gross[9]	Diasio (Satenstein)[7]	Scholtz (Bogen)
Corneum thickened	+	—	..	..	—
Acanthosis	..	+	+	..	+
Parakeratosis	+	—	+	+	+
Infiltration of epidermis	+	..	..	+	+
Dark friable masses between lamellae	+	..	..	..	..
Distortion of rete, especially of basal row	+	+	+	+	+
Empty spaces, vesicle formation ?	..	+	..	+	+
Scales and crusts	..	+	+	+	..
Thinning of granular layer	..	+	+	..	+
Edema of epidermis	..	+	+	+	+
Spongiosis	..	+	+	+	+
Intracellular edema (balloon degeneration)	+	+	..	..	+
Necrosis	..	..	+	+	..
Thinning of suprapapillary rete	..	+	..	..	..
Infiltrating cells, mainly lymphocytes and connective tissue cells	+	+	+	+	+

of parapsoriasis, as it is observed in varicella and seborrhea. It is curious that Mucha in his original description did not mention the disorganization of the basal layer.

All other histologic features singly or combined occur in several scaly dermatoses which are shown in table 2. Some of the histopathologic features cited by various workers as characteristic of parapsoriasis are found, as is aptly pointed out by Highman, in all inflammatory dermatoses. Such features are edema of the papillae of the corium, vascular dilatation and perivascular lymphocytic infiltration. Should some histopathologic resemblance between the Mucha-Habermann syndrome and parapsoriasis exist, it would be no more justifiable to point out the identity or nosologic relationship between these two conditions than to assert that tuberculosis and syphilis are identical or related nosologically on the basis of the histopathologic resemblance between tuberculous and syphilitic granulomas.

DIFFERENTIAL DIAGNOSIS

In most of the reported cases of the Mucha-Habermann syndrome a differentiation has been made and emphasized with regard to syphilis and tuberculids.

In my opinion the most characteristic morphologic feature of the new syndrome is that, as a composite whole, it does not fit in detailed analysis into any of the established dermatoses, while the individual lesions of the polymorphous eruption present considerable suggestive resemblance to several dermatoses.

The resemblance to a lenticular syphilid is suggested by the papular lesions. However, this resemblance is merely in general pictorial design. On detailed examination one has no difficulty in differentiating the lesions from syphilids because of their more superficial character, the brighter shade of red than the usual specific dull red, resembling the color of raw ham, and their distribution following the "bathing suit area" and sparing the forehead, face, palms and soles. The vesicular, hemorrhagic necrotic lesions, irrelevant history and negative serologic reactions complete the patent differences.

The same papular lesions bear resemblance to several psoriasiform dermatoses. The first is psoriasis. Psoriasis can easily be ruled out by the absence of the profuse mica-like desquamation, by the filmlike scale, by the lack of a deep infiltrated base and the papillary hemorrhages on scratching. Incidentally, the deep red, bare-looking lesions scattered on the trunk resemble psoriatic papules denuded of the scales; except that they have a dull red, waxy, lichenoid look.

Some of the papular lesions also strongly suggest seborrheic lesions by the waxy or greasy scale and its yellowish color; however, the scale is a trifle too dry and the papule is too deep and infiltrated for seborrhea. A diagnosis of seborrhea is also ruled out by the distribution, the guttate, discrete type of the lesions and the lack of any tendency to coalesce into larger patches.

Lichen planus hardly needs to be mentioned in the differentiation. The pictorial resemblance to the lichenoid type is suggested by the deep red and waxy appearance of some of the papular lesions bared and denuded of the scales, but the basic morphologic features of lichen planus, the polyangular flat papules, coalescence into rows or patches and itching are absent.

Varicella or the varioliform type has been emphasized sufficiently to be incorporated in the name. It is of interest that frank varicelliform or varioliform vesicles were noted and recorded in only a small minority of the cases reported. Most observers record merely a suggestion of the vesicles on the top of the papules. Fred Wise, whose descriptions are always clearly stated, detailed and precise, described vesicles as "vesicular formations, rather inconspicuous, deep seated, scaly tipped,

which would escape the examiner's eye and could have been easily overlooked unless one searched for them." The varioliform aspect of the lesions was suggested more by the presence of hemorrhagic and necrotic crusts, so often covering varicelliform and varioliform lesions and varioliform scars, than by the presence of the vesicles themselves.

With regard to the underlying etiology, two suggestions have been made. One, made by Drake, was that the condition might be of the tuberculid type. Some clinical resemblance and distribution probably prompted this suggestion. However, neither histopathologic nor immunologic observations corroborate this hypothesis. On the other hand, some assume that the condition might be attributed to some virus, suggesting pityriasis rosea or trichophytid. It must be admitted that the general morphologic picture (with the exception of the deep crusted necrotic lesions) and distribution convey a suggestion of pityriasis rosea. In this connection it is of interest to recall that vesicular lesions in pityriasis rosea have been reported by Klauder.[12]

A third suggestion of systemic toxins of variable nature is rendered plausible by the fact that in several cases systemic symptoms, such as subacute fever, headaches, general malaise, tonsillitis and intestinal disorders, were noted.

COMMENT AND CONCLUSIONS

Analyzing the histopathologic data advanced in favor of the identity of the Mucha-Habermann syndrome and parapsoriasis, one is justified in concluding that the evidence of histopathologic identity with, or at least close resemblance to, a dermatosis the histopathologic picture of which is regarded by the consensus of leading authorities as indefinite, uncertain and unreliable for diagnostic purposes is not solid and convincing enough to upset basic and fundamental clinical differences between the two dermatoses under consideration.

The only clinical points advanced for the identity of the two conditions deserving consideration are in a few isolated cases reported by Jadassohn, Rille, Arndt and Spiethoff, in which hemorrhagic and necrotic crusted lesions were mentioned as associated with parapsoriasis and in a few cases of Touton, Rusch[13] and Oppenheim[6] in which acute parapsoriasis merged into chronic, or vice versa. These reports are fragmentary and are not presented with detailed evidence bearing on the identity of the two types.

Granting even the clinical authenticity of the mixed lesions present, these cases are so few in comparison with the overwhelming number presenting clearcut lesions of one type or the other that their weight of argument is not sufficient to upset the clinical and histopathologic conception of parapsoriasis attained by a cumulative clinical experience

12. Klauder, J. V.: Pityriasis Rosea, J. A. M. A. **82**:178 (Jan. 19) 1924.
13. Rusch: Arch. f. Dermat. & Syph. **137**:32, 1921.

of many decades. In view of this it seems justifiable to leave open the question of the nosologic classification of the new syndrome. As to the name, it would seem rational and correct to name it simply the Mucha-Habermann syndrome.

Should one insist on a morphologically descriptive name, I suggest pityriasis varioliformis, a name commendable not only for its brevity but also because it emphasizes the two outstanding morphologic features accepted by all observers, scaling and the crusted varioliform aspect.

SUMMARY

The clinical features of this recently recognized entity are studied on the basis of previously published reports and new clinical observations, and their significance analyzed from the standpoint of general dermatologic concepts. The history of a case, the morphologic appearances and the laboratory findings are discussed with reference to etiologic, differential diagnostic and therapeutic considerations. Photographs of the gross appearance of the lesions and photomicrographs of histologic sections illustrate the clinical and pathologic observations.

DERMATITIS VENENATA FROM RHUS TOXIDODENDRON

REPORT OF UNUSUAL CASES

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Between May 29 and June 19, 1934, eight boys, ranging in age from 10 to 13 years, came to the outpatient department for cutaneous diseases of the C. V. Chapin Hospital with dermatitis of the forearms characterized by blisters of a sharp black color, varying in size from that of a pinhead to that of a pea. Some of

The forearms of two of the patients.

the lesions were broken, and some were in the linear formation usually seen in dermatitis caused by poison ivy. The black, blistered areas were conspicuously distinct on a background of moderately reddened skin (figure). The itching and discomfort were moderate. The duration was two days.

The first question asked the patients was whether a solution of silver nitrate or some other chemical had been applied to the raw surface. They said that no chemicals had been used. They stated that they had whipped one another with branches of Rhus toxidodendron.[1] Later they confessed that they had done this to be sent home from schcol.

1. The identity of the plant was established through the assistance of Dr. G. L. Church, of Brown University.

One of the patients had a few scattered black blisters and swelling of the genitals. Another had malaise for a few days. The rest complained of moderate itching and discomfort. The black stain came off with the subsequent peeling of the skin. Complete recovery followed in about four weeks.

I was unable to find the oxidized sap of Rhus toxidodendron mentioned among the numerous offending substances capable of producing dermatitis and a discoloration of the skin.

McNair [2] described the quick change of the colorless sap into a black sap when it is exposed to the air. An oxidized sap of this sort is supposed to be harmless. Descriptions in articles and textbooks of the symptomatology of dermatitis venenata from Rhus toxidodendron and other poisonous plants do not mention the possibility that black bullous dermatitis may arise from them.

As the injury was purposely inflicted, the cases also belong to the group of Dermatitis factitia.

184 Waterman Street.

2. McNair, J. B.: Rhus Dermatitis from Rhus Toxidodendron, Radicans and Diversiloba (Poison Ivy): Its Pathology and Chemotherapy, Chicago, The University of Chicago Press, 1923.

ERYTHROPLASIA OF THE GLANS PENIS (QUEYRAT)

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A relatively rare precancerous lesion was described as early as 1893 by Fournier and Darier.[1] This lesion occurred on the penis and was given the name, "épithéliome papillaire" or "épithéliome bénin syphiloïde de la verge." At a later date (1911), Queyrat[2] described in detail several cases of what was apparently an identical condition. Because of the color and the infiltration, and by comparison with leukoplakia in its tendency to become malignant, Queyrat proposed the name, "érythroplasie du gland." This name has persisted until the present time.

A case of erythroplasia was recently reported by Sulzberger and Satenstein,[3] in the discussion of which the literature was thoroughly reviewed. Although these authors discovered about forty cases, none were found in the American literature, their case being unique in this respect.

Although the original descriptions deal with penile lesions, subsequent cases have appeared in which the lesions occurred on the vulva, clitoris and buccal mucosa, and even on the skin. Many cases described have occurred in syphilitic patients, but the presence of syphilis is not necessary for the diagnosis of erythroplasia.

Shortly after the publication of the paper by Sulzberger and Satenstein, a patient presenting himself at this clinic had a penile lesion which was undoubtedly an example of erythroplasia. More recently, a case was presented before the New York Dermatological Society for diagnosis, most discussers favoring a diagnosis of erythroplasia.[4]

In view of the rarity of this condition and until recently its absence from the American literature, it seems worth while to submit the following case.

REPORT OF A CASE

History.—A white man, aged 42, was referred to this clinic from Ypsilanti State Hospital for diagnosis and treatment of a penile lesion. There was his-

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Studies and Contributions from the Department of Dermatology and Syphilology, University of Michigan Medical School, service of Dr. Udo J. Wile.

1. Fournier, A., and Darier, J.: Epithéliome bénin syphiloïde de la verge, Bull. Soc. franç. de dermat. et syph. **4**:324, 1893.

2. Queyrat: Erythroplasie du gland, Bull. Soc. franç. de dermat. et syph. **22**:378, 1911.

3. Sulzberger, M. B., and Satenstein, D. L.: Erythroplasia of Queyrat, Arch. Dermat. & Syph. **28**:798 (Dec.) 1933.

4. Throne, Binford: A Case for Diagnosis, Arch. Dermat. & Syph. **29**: 633 (April) 1934.

tory of a chancre twenty years ago, which was burned off. No antisyphilitic therapy was given, and there were no further symptoms until two years ago, at which time the patient became nervous and irritable. In March 1933, the patient was examined at another hospital. He had contracted gonorrhea following frequent exposures. Serologic tests of the blood and of the spinal fluid gave positive results, and the patient was given one intravenous injection and pills by mouth. He was then transferred to the Ypsilanti State Hospital with a diagnosis of dementia paralytica.

At this time, March 17, 1933, the penile lesion was first noticed. Because of the confused mental state of the patient, the duration of the lesion could not be determined. A specimen was taken for biopsy and a report of syphilis was made by a general pathologist. A urologist, called into consultation, expressed the opinion that the lesion was pyogenic and advised a dusting powder locally. The

Fig. 1.—The lesion as it originally appeared. The velvety appearance, irregular border, infiltration and thickened prepuce are easily seen.

only other treatment had consisted of intravenous injections of arsphenamine and malaria therapy. No history could be elicited of ingestion of phenolphthalein or other drugs. The past and family histories revealed no pertinent information.

Examination (Jan. 1, 1934).—The patient, a well developed and well nourished white man, presented all of the classic clinical signs of dementia paralytica, but otherwise was well.

He had two lesions, one of which occupied the right side of the nose near the inner canthus of the eye and was obviously a small carcinoma, while the other consisted of a dully erythematous, infiltrated plaque with an irregular border and a velvety surface involving the glans, the sulcus coronarius and the adjacent inner surface of the prepuce, but sparing the meatus. It was firm to palpation and felt somewhat sclerotic. The surface was moist and velvety and presented a few small erosions. The inner surface of the prepuce was thickened and not

as freely movable as is normal. The prepuce was adherent to the under surface of the glans near the frenum. The lesion was slightly painful on manipulation.

Treatment.—Circumcision was performed, followed by thorough destruction of the lesion by actual cautery. The wound healed satisfactorily. The patient was then discharged and has not returned for further observation.

Microscopic Examination.—The histologic section from the glans penis revealed an unusual picture. Low power magnification showed an irregular acanthosis, the rete pegs being irregular in shape and size. The epidermis overlying the papillae between the rete pegs was only the thickness of a few cells in many places. There were many cells in the lower portion of the epidermis hav-

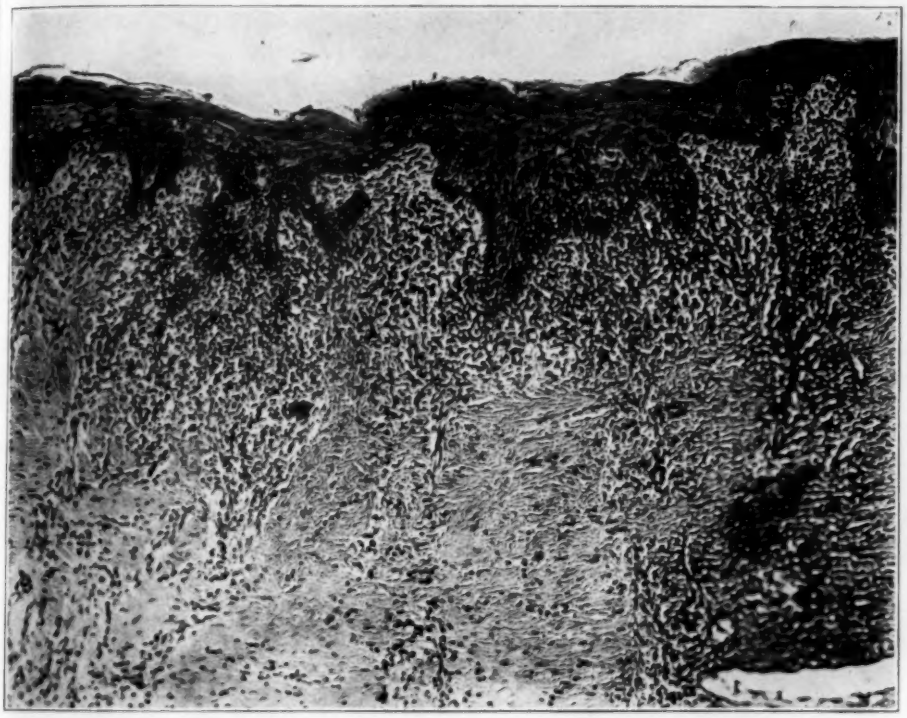

Fig. 2.—Low power photomicrograph showing irregular acanthosis, cellular infiltrate and dilated vessels in the corium.

ing a vacuolar appearance under this magnification. The stratum granulosum, stratum lucidum and stratum corneum were not discernible over this portion of tissue, but were present and normal in appearance at either end of the section where the underlying pathologic process was less pronounced.

The corium presented irregularly shaped papillae corresponding with the irregularities of the epidermis. Many irregular portions of papillae were either completely or partially enclosed by downward and lateral projections of the epidermis. There was a fairly dense cellular infiltrate of small round cells occupying the papillary and subpapillary layers of the corium. Deeper in the corium many blood vessels and lymph spaces could be seen, and there was a moderate perivascular infiltration of lymphoid cells.

With high power magnification, the hyperplasia of the epidermis was seen to be due chiefly to an increase in the number of prickle cells, although in many places there were several layers of columnal basal cells. A few of the basal cells and many of the overlying prickle cells contained clear oval vacuoles which occupied a large portion of the cell, pushing the nucleus to one side. In the middle and upper portions of the epidermis, the prickle cells appeared shrunken, leaving a clear zone surrounding the cytoplasm. Many of the nuclei were sickle-shaped. A few lymphocytes had migrated into the epidermis. Under this magnification, the stratum granulosum was seen, but the cells were less distinct than normal and contained fewer granules. Occasional clear spaces appeared in the prickle cell layer, containing the remains of cellular material. Occasional mitotic figures were seen.

Fig. 3.—High power photomicrograph showing pyknosis and vacuolation in the prickle cells as well as a few mitoses.

The infiltrate in the corium was seen to be chiefly lymphocytic, as was also the perivascular infiltrate deeper in the section. A few plasma cells but no giant cells were seen.

COMMENT

The suspicion that this case was one of erythroplasia, based on the gross appearance of the lesion, was verified by the microscopic picture which agreed in all essential details with the original descriptions by Queyrat and the recent case described by Sulzberger and Satenstein.

MUCOR PARONYCHIA

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AND
O. A. PLUNKETT, PH.D.
LOS ANGELES

This concluding report deals primarily with the classification of a fungus which was isolated from the nails of certain orange workers and reported in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY in 1929 under the title of "Paronychia." [1]

The following brief data are supplied as to (1) the reaction of the orange host and (2) the tenacity of life of this species of Mucor.

The fact that several weeks could elapse without external or visible evidence of infestation in the orange following inoculation led us to investigate how long the oranges would be considered fit for human consumption after acquiring the disease, and to this end several healthy oranges were inoculated by pulp stabs under sterile conditions. All manifested similar phenomena: There was a slow diminution in size, accompanied by softening, with a gradual loss of weight, and after about four months had elapsed, the oranges affected demonstrated an equally slow hardening and a change of color to yellow-brown. Even at this stage the orange could still be accepted by the uninitiated as the stunted orange known to the trade as a cull. It must not be assumed that culls in general are due to this fungus, as of the many culls haphazardly picked, sectioned and searched by us, positive findings of a similary morphologic fungus were made in only a few instances. Because of the rarity of their occurrence and because of the work entailed the fungi were not proved.

Rapid destruction never follows this Mucor infection. There results a rather slow progression from the point of inoculation throughout the pulp of the orange. The former article [1] demonstrated the cross-section of an infected orange in which it could be seen that only the segment punctured was involved. Later cuts showed that there occurred an advancing destruction of the adjoining fibrous septums. The pulp cells

1. Sutherland-Campbell, H.: Paronychia: An Attempt to Prove the Etiologic Factor in an Epidemic Among Orange Workers, Arch. Dermat. & Syph. **19**:233 (Feb.) 1929.

enlarged and ruptured, thus liberating the sugary solution which accounts for the external manifestation of softening. There followed a gradual absorption of the liquid, with a consequent dehydration of all of the tissues as the interior became exhausted. The result was a mummified shell, scrapings from the empty interior of which gave for many months afterward vigorous growths of the fungus on Sabouraud's mediums. The marked resistance manifested by the skin of the orange indicated that the infections in the first instance were due possibly to an inclusion which dated from pollination rather than to a more recent trauma, which would of necessity involve the skin and which always results experimentally and under normal conditions of exposure in rapid infestation and early destruction by the blue mold. The contrast in the weight and the appearance of the oranges before and after dehydration is of interest (fig. 1).

Fig. 1.—Comparison of normal and ingested oranges. The normal weight is 230 Gm.; the weight after ingestion, 15 Gm.

TENACITY OF LIFE

The fungus was cultivated for many generations on Sabouraud's mediums at room temperature. The only changes noted were a somewhat lessened capacity for aerial growth with age and variation in the color from almost white in the early growth to a dirty brown in the very old growth. Several early vigorous growths were sealed off in test tubes as follows: After the slant was inoculated the cotton plugs were dipped into plain white wax before being reinserted; next they were covered with a heavy coat of sealing wax. The tubes were then kept at room temperature for varying periods of time. Dehydration of the mediums generally took place in about five months. The usual changes in aerial mycelial formation and color concomitant with age took place; as the mediums became hard and black a further shrinkage was observed, until at last only small clumps of brownish masses were left clinging to the hardened slant. The walls of the tube were gradually covered with spores which simulated a dirty, brownish dust. The tubes

were opened at varying periods of time after six months had elapsed. Scrapings were taken and planted on fresh slants of Sabouraud's mediums. The first implants gave positive growths from scrapings from the surface of the hardened slants; but as the length of time elapsing without food increased, the slants which were hard, dry and brittle, had to be buried in their entirety in order to obtain growths. This occurred in all of the slants over 2 years old. The slant which was buried last and which gave a positive growth was planted five years after being sealed; it existed without foodstuffs for approximately four and one-half years, as it took the slant about five or six months to dry out after implantation. The further observation may roughly be made that in general the longer the fungus was left without food, the longer the latent period was before visible growth could be obtained following the replanting. The maximum latent period was eleven days. The growths, especially the later ones, manifested a distinct change in vitality, only a brownish granular scum being observed in the first generation. Several transplants had to be made before there was again a reversion to type. Photographs demonstrating these phenomena were made.

A series of dish cultures manifested a definite retardation of growth with an attenuation and diminution of aerial hyphae under weekly doses of roentgen rays as small as one-eighth skin unit, but there was no destruction of the fungus following this or following individual doses as high as 7 skin units. This species of Mucor thus shows a marked tenacity of life when compared with many other fungi, some of which die out rather readily on artificial mediums. Experiments on lethal hot and cold extremes have not yet been attempted.

NATURE AND IDENTITY OF MUCOR CAUSING PARONYCHIA

In 1928, Dr. H. Sutherland-Campbell [1] brought to our attention a species of Mucor isolated from several patients who had paronychia. In all of the cases the patients were employed in plants manufacturing orange products, where their hands were frequently in orange juice. No attempt was made at that time to identify the organism beyond the genus. The occurrence of the organism in cases of paronychia and the fact that the same organism had been isolated from cull oranges as well as from diseased nails warranted a further classification of this fungus.

The genus Mucor Micheli [2] is the largest in the Mucorales, more than one hundred and fifty species being listed and described in Sac-

2. Micheli, P. A.: Nova plantarum genera, Florentiae, typis B. Paperinii, 1729, p. 215.

cardo's "Sylloge fungorum."[3] Mucor is closely related to the genus Rhizopus, but is readily differentiated by the absence of runners or stolons, so prevalent and characteristic of Rhizopus. The growth of Rhizopus fills the Petri dish more rapidly than does Mucor and because of the rhizoids is able to climb up the sides and over the top of the dish. Mucors cover the surface of the medium with mycelial growth, but because of the absence of rhizoids do not attach themselves to the lid. The sporangiophores of Rhizopus arise from the nodes of the stolons, while in Mucor the sporangiophores arise from all parts of the mycelium. In Mucor the columella is continuous with the sporangiophore, while in Rhizopus it rests in a cup-shaped expansion of the sporangiophore called the apophysis.

The following generic description of Mucor is that given by Fitzpatrick[4] in 1930:

> Mucor Micheli, in Nova Plantarum Genera, p. 215, pl. 95, 1729; also see Link in Linnaeus' Species Plantarum (4 edit.) **6**:80, 1824. Syn. Hydrophora Tode (Fung, Meckl.) **2**:5, 1791. Mycelium develops profusely both in and on the substratum; lacking definite rhizoids and stolons, sporangiophores not fasciculate as in Rhizopus, arising singly from the mycelium, erect, simple or somewhat branched in a monopodial or sympodial manner; all the branches terminated by sporangia; sporangia large, globose, many-spored; sporangial wall evanescent in most species, not cutinized, more or less incrusted with crystals of calcium oxalate; columella always present, various in shape; sporangiospores globose to ellipsoidal, with a thin, smooth wall; zygospores borne on the mycelium; suspensors lacking outgrowths; copulating branches lying end to end, forming a straight line, not having the tongs-like aspect seen in certain other genera; terminal or intercalary, smooth, hyaline chlamydospores found in some species.

The genus has always been difficult for taxonomists to distinguish because of the apparently large number of species and the pleomorphic forms that obtain when the fungus is grown on different substrata. The older descriptions are too brief and inadequate to be of determining value. Herbarium specimens, where they exist, are too fragmentary and worn to be of any use in diagnosis.

In his monograph of fifty-one species of Swiss Mucor Lendner[5] gave the most useful diagnosis of species. He used as characters for classification the branching on the sporangiophores, their height and thickness, the shape and size of the columella, the degree of diffluence of the sporangium membrane and the size and shape of the spores.

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3. Saccardo, P. A.: Sylloge fungorum omnium huiusque cognitorum, Patavii, sumptibus auctoris, 1882-1931.

4. Fitzpatrick, H. M.: The Lower Fungi: Phycomycetes, New York, McGraw-Hill Book Company, 1930.

5. Lendner, A.: Les mucorinées de la Suisse, in Beiträge zur Kryptogamenflora der Schweiz, Bern, K. J. Wyss, 1908, vol. 3, pt. 1.

In his analytic key to the species of Mucor, Lendner followed the arrangement of Fischer [6] for his three large groups: (1) Monomucors with unbranched sporangiophores, (2) Racemucors with branches in racemes or corymbs and (3) Cymomucors with branches in sympodial cymes.

Any one who has attempted to use Lendner's key has found difficulty in determining whether the sporangiophores are branched or unbranched and whether they are racemosely or cymosely branched. In a great many species the age of the culture and the nature of the substratum have a decided influence on the nature and the size of the sporangiophores. There are species in which all types of branching are met with; different students place the same species under different types of branching.

Povah [7] attempted to separate the species of Mucor by growing them on a uniform standard bread culture. He used the height of the turf, the color of the turf, the spore form and the nature and the form of the columella as diagnostic characters. For the eighteen American species which he studied, his plan seems to be successful.

Of the many species of Mucor described there are only a few listed as parasites of man or animals. Of these Mucor corymbifer Cohn, Mucor ramosus Lindt, Mucor pusillus Lindt, Mucor racemosus Fresenius and Mucor mucedo (Linnaeus) Brefeld are those commonly encountered. Infection with these organisms is usually associated with otomycoses and pulmonary lesions. We have been unable to find reference to any species of Mucor associated with paronychia.

In Seymour's "Host Index of the Fungi of North America" [8] (1929), mention is made of Mucor clavatus Link as occurring on an unknown species of citrus. According to Fischer [9] Link's species is not valid and is merely a form of Rhizopus nigricans Ehrenburg.

Mucor griseus Bonard has been found on Citrus aurantium in Europe.[10] This species is given as being synonymous with M. racemosus Fresenius. The only Mucor found in the literature occurring both on citrus and on man is therefore M. racemosus Fresenius.

The present organism was studied morphologically on a number of mediums and compared with various authentically described species, following in general the methods employed by Povah.[7] From this

6. Fischer, A.: Phycomycetes, in Die Pilze Deutschlands, Österreichs und der Schweiz, Leipzig, E. Kummer, 1892, vol. 4.

7. Povah, A. H. W.: A Critical Study of Certain Species of Mucor, Bull. Torrey Bot. Club **44**:241 and 287, 1917.

8. Seymour, A. B.: Host Index of Fungi of North America, Cambridge, Mass., Harvard University Press, 1929.

9. Fischer,[5] vol. 1, pt. 4, p. 232.

10. Saccardo,[3] vol. 7, p. 194.

study it was decided that none of the existing species were in close enough agreement to permit the inclusion of the present form; a new species with the following description is proposed:

MUCOR PARONYCHIUS (NEW SPECIES)

Mucor paronychius forms on bread a loose mouse-gray turf, from 5 mm. to 1 cm. in height. The sporangiophores are of two kinds—tall and short; the tall sporangiophores finally collapse and form a weft over the short ones, and the short sporangiophores form a dense layer on the substratum. The tall sporangiophores are from 8 to 11 microns in diameter, with short lateral branches; the short sporangiophores are from 10 to 15 microns in diameter and variously, often somewhat circinately, branched. The globose sporangia are from 35 to 65 microns in diameter and are at first white, later becoming yellowish brown and finally lightly encrusted with crystals; the sporangium wall is deliquescent, leaving a small basal collar around the columella, or persistent and irregularly ruptured; the columellas are free, oval or pyriform, but usually oval, and from 18 to 28 by from 25 to 40 microns without contents. The sporangiophores are spherical and from 4 to 6 microns in diameter or oval and from 3 to 4 by 5 to 7 microns. They are pale gray in mass. Zygospores are unknown. The chlamydospores are of two kinds: (1) the microchlamydospores, which are born in the sporangiophores and are oval or oblong, somewhat blunt at the ends and from 10 to 11 by 12 to 15 microns or sometimes spherical and from 11 to 13 microns in diameter; the contents are less granular and their walls are thinner than those of (2) the macrochlamydospores, which are born in the vegetative mycelium and are oval or spherical and from 14 to 18 microns in diameter, with thick walls and a densely granular content. Both types of chlamydospores are colorless. Oidia are formed in liquid mediums containing sugars, in oranges and in human finger-nails. This parasite fungus is found in human finger-nails frequently saturated with orange juice and in cull oranges.

Systematic Relationship.—M. paronychius is similar to M. racemosus Fresenius in the production of oidia and chlamydospores. The aerial sporangiophores produced on sterilized orange have a similar branching and production of chlamydospores. The species differ in the nature and the size of the chlamydospores, since those of M. racemosus Fresenius remain barrel-shaped and are jet black. Mucor erectus Bainer and Mucor fragilis Bainer, two species closely related to M. rasemosus Fresenius, differ from the present species in the nature of the spores and columella. In M. fragilis the spores are smaller, oval (4.2 by 2.1 microns) and bluish gray, while in M. erectus the spores are elongated (from 2.5 to 5 by from 5 to 10 microns). Of the various species from North America

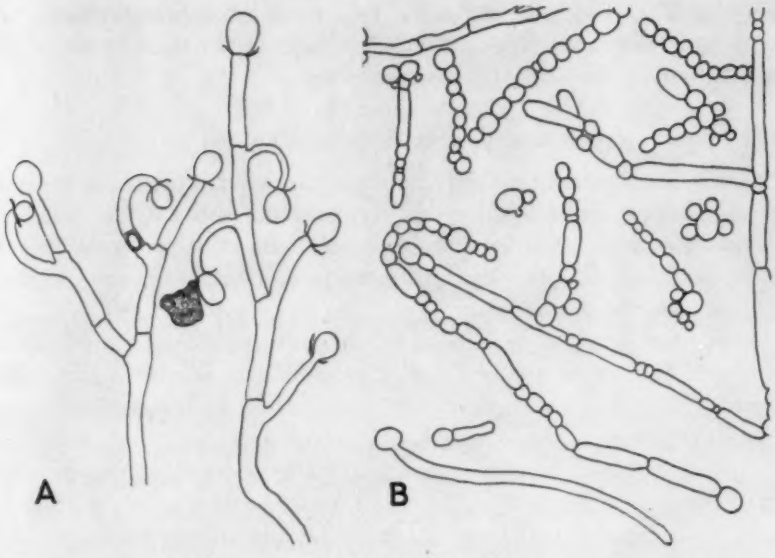

Fig. 2.—*A*, sporangiophores demonstrating the branching and columellae, and *B*, the oidial form in anaerobic growths in oranges.

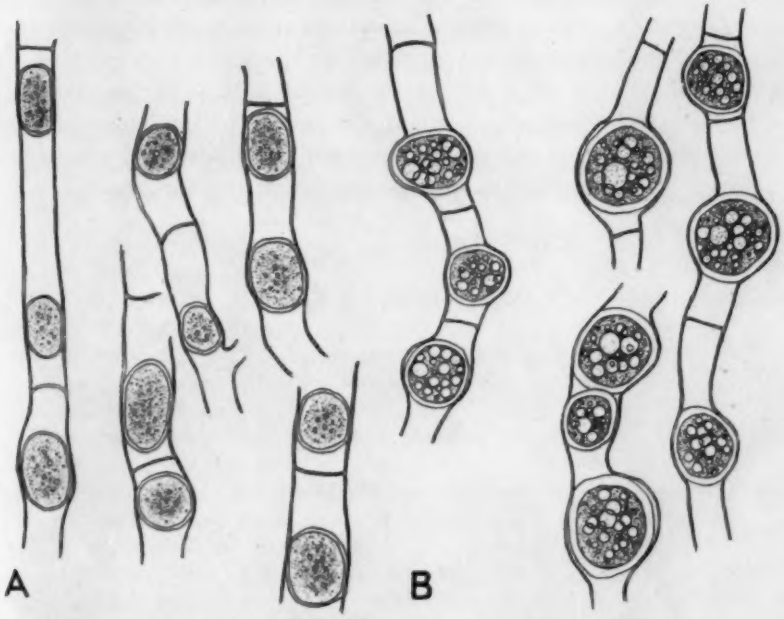

Fig. 3.—*A*, a microchlamydospore born in a sporangiophore, and *B*, a macrochlamydospore born in a vegetative mycelium.

listed by Povah [7] M. paronychius most closely approaches Mucor circinelloides Van Tieghem in having two types of sporangiophores but differs in having two types of chlamydospores, in the nature of the columella and of the size of sporangiospores.

CULTURAL NOTES AND OBSERVATIONS

To test the fermenting ability of the organism it was grown in carbohydrate peptone broth solutions in fermentation tubes. The following carbohydrates were used in 1 per cent solutions in 10 per cent peptone broth: dextrose, lactose, levulose, galactose, dextrin, inulin, maltose, soluble starch and orange juice.

The organism grew well in all of the cultures except soluble starch and inulin, the inulin giving a better growth than soluble starch. The growth consisted of a well developed surface mat with considerable submerged mycelium, the submerged mycelium producing numerous chlamydospores and oidia in all cases. Dextrose, levulose, galactose and orange juice were fermented, 50 cc. of dextrose broth giving 15 cc. of gas; a similar quantity of levulose, galactose and orange juice gave from 5 to 7 cc. of gas.

When inoculated into Valencia oranges, growth occurs within the pulp with a slight amount of mycelium and an abundance of budding oidial production. After prolonged anaerobic growth of the fungus the orange becomes mummified without showing any external evidence of the fungus except a small weft of mycelium at the point of inoculation. The peel of the orange is not softened or digested, showing that the fungus is inhibited in its action by the volatile oils of the peel. When the fungus is inoculated into a lemon, the outside of the lemon becomes covered with mycelium and sporangiophores and is decayed with a soft rot. In this case the volatile oil does not inhibit the fungus.

VERRUCAE

A REVIEW

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AND
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Verruca vulgaris and verruca plana juvenilis are classified by Jadassohn [1] among the benign epitheliomas of infectious origin. The filiform wart of the face and scalp is closely related, and there is good evidence for classifying condyloma acuminatum in this group. The plantar wart is probably of the same etiology, although this relationship has not been demonstrated experimentally. Experiments by Ullman,[2] not yet repeated by other observers, suggest that the papilloma of the larynx of childhood may fall in the same group. The relationship between the various types has been demonstrated by the production of verruca vulgaris and verruca plana juvenilis from condyloma acuminatum and from filiform warts,[3] and by the production of verruca plana juvenilis from material derived from a laryngeal papilloma.[2]

Frey [3a] discussed the relationship between warts and condyloma acuminatum. Two thirds of the patients with condyloma that he observed were free from syphilis, gonorrhea or other genito-urinary disturbance, and 50 per cent had or had had common warts. Dubreuilh [4] stated that warts on the hands do not occur with plantar warts, but we have observed from one to three verrucae on the hands of 5 of 14 patients carefully examined with this in mind. Patients with numerous verrucae vulgares are occasionally found also to have plantar warts.

From the clinic for cutaneous diseases, service of Dr. E. L. Oliver, Massachusetts General Hospital.

1. Jadassohn, J.: Die benignen Epitheliomen, Arch. f. Dermat. u. Syph. **117**: 577, 705, 833, 1913-1914.

2. Ullman, E. V.: (*a*) Experimentelle Ueberimpfung von Larynxpapillomen, Monatschr. f. Ohrenh. **56**:884 (Nov.) 1922; (*b*) Report of paper read at the Gesellschaft der Aerzte in Vienna, Wien. klin. Wchnschr. **34**:599 (Dec. 8) 1921; (*c*) Uebertragungsversuche bei Kehlkopfpapillomen, Monatschr. f. Ohrenh. **55**:1717 (Dec.) 1921.

3. (*a*) Frey, E.: Zur Frage der aetiologischen Beziehung der Warzen und spitzen Kondylomen, Schweiz. med. Wchnschr. **5**:215 (Feb. 28); **5**:239 (March 6) 1924. (*b*) Serra, A.: Studi sul virus della verruca, del papillome, del condiloma acuminato, Gior. ital. d. mal. ven. **65**:1808 (Dec.) 1924. (*c*) Waelsch, L.: Uebertragungsversuche mit spitzen Kondylomen, Arch. f. Dermat. u. Syph. **124**: 625, 1917.

4. Dubreuilh, W.: Contribution à l'étude clinique de la verrue plantaire, Ann. de dermat. et syph. **6**:441, 1895.

Warts also occur in cattle (usually on the teats or the udder of cattle and on the head, sides of the neck and shoulders of yearlings), in dogs (for the most part on the buccal or vaginal mucous membrane, but also more rarely on the skin) and in horses (small mucous membrane or cutaneous lesions).[5] Neither in man nor in animals, however, has the natural history of these lesions been studied satisfactorily. That they disappear spontaneously is generally admitted. Artificially produced warts disappear spontaneously, as a rule in from a few weeks to seven months.[6] In the one available study of natural warts [7] it was found that of 70 subjects with verruca vulgaris and verruca plana juvenilis 2 were free from warts in from two weeks to a month, 5 were free in from two to three months and a total of 20 were free in six months. The warts of cattle generally clear up spontaneously when the animals reach the adult age, but this is not invariable.

The contagiousness of warts and condylomas has been definitely established, both by observations of accidental transmission and by experimental transmission by the intracutaneous inoculation of finely ground wart material, first by Jadassohn, in 1895, then by numerous other experimenters.[8] It has been established that the warts of cows, dogs and horses are also contagious.[9] An epidemic of warts on the

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5. (*a*) Creech, G. T.: Experimental Studies of the Etiology of Common Warts of Cattle, J. Agric. Research **39**:723 (Nov. 15) 1929. (*b*) M'Fadyean, J., and Hobday, F.: Note on the Experimental Transmission of Warts in the Dog, J. Comp. Path. & Therap. **2**:341 (Dec. 31) 1898. (*c*) Royère, J.: Des verrues chez l'homme et chez les animaux, Thèse de Lyon, 1902.

6. (*a*) Jadassohn, J.: Sind die Verrucae Vulgares übertragbar? Verhandl. d. deutsch. dermat. Gesellsch. **5**:497, 1896. (*b*) Tuccio, G., and Cappolino, C.: Inoculazioni di verruche filiformi, Gior. ital. d. mal. ven. **53**:398, 1912. (*c*) Creech.[5a] (*d*) M'Fadyean and Hobday.[5b]

7. Memmesheimer, A. M., and Eisenlohr, E.: Untersuchungen über die Suggestivbehandlung der Warzen, Dermat. Ztschr. **62**:63 (Sept.) 1931.

8. Lanz, O.: Ein Beitrag zur Frage der Uebertragbarkeit von Warzen, Cor.-Bl. f. schweiz. Aerzte **28**:264 (May 1) 1898; Experimentelle Beiträge zur Geschwulstlehre, Deutsche med. Wchnschr. **25**:313 (May 18) 1899. Licht: Die Ansteckungsfähigkeit der Warzen, Ugesk. f. læger **1**:368, 1894; abstr., Deutsch. med.-Ztg., Aug. 12, 1895, p. 730. Neisser, A.: Ueber das Epithelioma (sive Molluscum) contagiosum, Vrtljschr. f. Dermat. u. Syph. **15**:553, 1888 (note, p. 575, statement on the contagiousness of common warts). Variot, G.: Un cas d'inoculation expérimentale des verrues de l'enfant à l'homme, J. de clin. et de thérap. inf. **2**:229 (June 21) 1894. Vivès, M.: Verrues de famille, J. d. mal. cutan. **11**:463 (Aug.) 1899. Ullman.[2b] Waelsch.[3c] Jadassohn.[6a] Tuccio.[6b]

9. (*a*) Schultz, F.: Experimentelle Uebertragung von Verrucae vulgares vom Rinde auf den Menschen mit ausserordentlich langer Inkubation, Deutsche med. Wchnschr. **34**:423 (March 5) 1908. (*b*) Schindelka, in von Bayer, J., and Fröhner, E.: Handbuch der tierärztlichen Chirurgie und Geburtshilfe, Vienna, Wilhelm Braumüller, 1899-1908, vol. 6, quoted by Schultz.[9a] (*c*) M'Fadyean and Hobday.[5b] (*d*) Royère.[5c]

oral mucous membrane of an entire kennel of dogs has been reported.[10] Although transfer between species is difficult, warts have been passed from man to a cow's udder, from a cow's udder to man, with an incubation period of three years; from man to the buccal and vaginal mucous membrane of dogs and, lastly, from cattle to guinea-pigs, with the production of atypical lesions.[11]

Hyperkeratoses grossly and histologically similar to warts may be produced by foreign bodies. Thus, it is reported in one instance that small splinters of glass were responsible for warts that regressed only when the splinters were removed.[12] Dewirtz [13] reported histologically typical warts on the palmar surface of hands and fingers and on the soles of asbestos workers. He found that these warts are always caused by a splinter of asbestos, and that they always clear up immediately on removal of the foreign body. Montgomery [14] found that flat feet, hyperhidrosis and plantar warts are frequently found together. Wile and Kingery,[15] while they did not deny that trauma or foreign bodies may cause warts, expressed the opinion that it is more likely that the infectious agent is also present.

From about 1880 to the time of the first demonstration of the virus there was much speculation concerning the bacterial origin of warts, various organisms being proposed as the etiologic agent. In 1907, Ciuffo [16] first demonstrated that warts could be produced by the inoculation, on a scarified area, of a sterile filtrate of ground up warts, the incubation period being about five months. In 1908, Serra [17] confirmed this observation, although he failed to get any results with material from filiform warts or condylomas. In 1924, however, Serra reported success with material from these two sources, typical common warts being produced in one third of the subjects inoculated. Again the

10. Penberthy, J.: Contagious Warty Tumors in Dogs, J. Comp. Path. & Therap. **2**:363 (Dec. 31) 1898.

11. Soule, M. H., and McKinley, E. B.: Experimental Inoculation of Man and Guinea Pigs with the Virus of Cattle Warts, Proc. Soc. Exper. Biol. & Med. **28**:1027 (June) 1931.

12. Schall: Zur Aetiologie der Hautwarzen, Arch. f. Dermat. u. Syph. **35**: 207, 1896.

13. Dewirtz, A. P.: Asbestwarzen, Arch. f. Dermat. u. Syph. **161**:1 (Jan.) 1930.

14. Montgomery, D. W.: The Etiology of Verruca, J. A. M. A. **56**:1193 (April 22) 1911.

15. Wile, U. J., and Kingery, L. B.: The Etiology of Common Warts, J. A. M. A. **73**:970 (Sept. 27) 1919.

16. Ciuffo, G.: Innesto positivo con filtrato di verruca volgare, Gior. ital. d. mal. ven. **48**:12, 1907.

17. Serra, A.: Ricerche istologiche e sperimentali sul condiloma acuminato, i papillomi del capo e la verruca volgare: Contributo all'etiologia, patogenesi, filtrabilità, Gior. ital. d. mal ven. **49**:11, 1908.

incubation period was about five months. Wile and Kingery,[15] in 1919, repeated Ciuffo's work, injecting the sterile filtrate intracutaneously. In from four to seven weeks small flat warts appeared, grew slowly and, for the most part, disappeared spontaneously. The only one which reached a large size and a small one were typical histologically. Control experiments with filtrate from normal epithelium gave negative results. Injections of sterile filtered material preserved in glycerin for five weeks also gave negative results. With a sterile filtrate prepared from an artificially produced wart, Kingery [18] produced warts of the second generation which were histologically typical. Creech [5a] produced warts on calves, and transferred them from calf to calf by the intracutaneous injection of both filtered and unfiltered material. Of twenty-two attempts at transfer, fifteen gave positive results, the unfiltered material giving a slightly higher percentage of success. The incubation period was from one to three months, and the warts for the most part disappeared spontaneously by the seventh month. Thus, the evidence that warts are caused by a filtrable virus is fairly conclusive, unless one agrees with Bonjour [19] that the success of experiments of transmission is due to suggestion. These experiments in transmission are the sum of the present knowledge of the virus. To quote Findlay,[20] "Nothing of the reaction of the virus of warts to chemical or physical agents is known except that it withstands the action of 50 per cent glycerine."

EXPERIMENTAL WORK

In an unsuccessful effort to uncover further facts concerning the virus, the intracerebral inoculation of eight guinea-pigs with ground up wart material was carried out under the direction of Dr. Louis Dienes. Seven of the eight animals survived the operation, and all were watched for three months. Gross and microscopic examinations of the brains of two of the animals showed no abnormalties (done by Dr. Charles Kubik). None showed signs or symptoms of involvement of the central nervous system.

The procedure in these experiments was as follows:

The warts used as material were removed from patients and used within from three to thirty hours, being kept in a sterile test tube in an ice-box in the interim. Both verruca vulgaris removed from the back of hands or fingers and filiform warts removed from the chin and lips were used. First the warts were cleansed

18. Kingery, L. B.: The Etiology of Common Warts: Their Production in the Second Generation, J. A. M. A. **76**:440 (Feb. 12) 1921.

19. Bonjour, J.: Mise en point sur la rôle de la suggestion, Presse méd. **37**: 1210 (Sept. 14) 1929.

20. Findlay, G. M.: Warts, in Medical Research Council: A System of Bacteriology in Relation to Medicine, London, His Majesty's Stationery Office, 1930, vol. 7 chap. 18.

with 70 per cent alcohol; then procaine hydrochloride with epinephrine was injected under them; then they were removed by curet and transferred to a sterile test tube. Just before injection the material was transferred to a sterile mortar, a few drops of sterile physiologic solution of sodium chloride was added, and the wart was thoroughly ground. The guinea-pig was given ether, a small incision (about 1 cm. in length) was made over the cranial vault, and a small hole was bored in the skull by means of a hand drill equipped with a guard to prevent the bit from damaging the brain when through the skull. Through the opening thus produced, about 0.5 cc. of ground up material was injected into the brain, and the wound was closed with two or three skin clips. Both male and female animals were used.

While the results of these experiments were entirely negative we feel that work along this and similar lines will be productive of important fundamental facts about the virus. Especially valuable would be the discovery of an animal which would respond to the virus in some fashion without the long incubation period which hampers investigation by the present means of transfer.

THERAPY

The lack of controlled investigations and the generally admitted spontaneous disappearance of warts make the question of therapy a confused one. So far as we know in only one instance was a group given treatment while, as a control, a similar group was given no treatment. This was reported by Memmesheimer and Eisenlohr.[7] Seventy cases of verruca vulgaris and verruca plana juvenilis were inspected one-half, one, three and six months after the warts were first seen. At the end of that time 20 subjects (28.5 per cent) had no warts. Data on a much larger series are needed before such a figure can be accepted without question, but it indicates that a considerable proportion of subjects will be found to be cured if followed for a long enough time.

Perhaps the most effective and the most commonly used treatment for warts when occurring singly or in small numbers is radium or roentgen rays or a combination of both.[21] There are, however, no

21. (*a*) Barcat, M.: Verrues planes traitées par le radium, Bull. Soc. franç. de dermat et syph. **21**:172 (July 7) 1910. (*b*) Brünauer, S.: Zur Strahlenbehandlung der Warzen, Strahlentherapie **29**:255 (June 30) 1928. (*c*) Degrais, P., and Bellot, A.: La verrue plantaire: avantages de son traitement par le radium, Presse méd. **39**:1840 (Dec. 12) 1931. (*d*) Fox, H.: The Roentgen Ray in the Treatment of Skin Diseases, Arch. Dermat. & Syph. **9**:13 (Jan.) 1924. (*e*) Fox, H.: Warts, Moles and Corns, Am. J. Surg. **6**:418 (April) 1929. (*f*) Hazen, H. H.: Roentgen-Ray and Radium Treatment of Plantar Warts, Am. J. Roentgenol. **19**:440 (May) 1928. (*g*) Hazen, H. H., and Eichenlaub, F. J.: The Roentgen-Ray Treatment of Verruca Plantaris, J. A. M. A. **74**:1311 (May 8) 1920. (*h*) Juster, M. E.: Les traitements pratiques des verrues, J. de méd. de Paris **47**:837 (Oct. 18) 1928. (*i*) McCafferty, L. K., and McCarthy, C. L.: The X-Ray Treatment of Callositas and Verruca Plantaris, with Some Remarks on

(Footnote continued on next page)

controlled groups, so that the part played by spontaneous disappearance cannot be estimated. On the whole, from 80 to 90 per cent of subjects are reported cured by these means, over 90 per cent when both are used.

Surgical treatment need not be discussed. The recurrence of plantar warts after excision is well known. All varieties of caustic chemicals have been used in therapy and recommended. Freezing with ethyl chloride [22] or carbon dioxide snow,[23] the application of a 40 per cent solution of calcium phosphate or calcium carbonate in hydrous wool fat,[24] salicylic acid in various vehicles, sodium bisulphite,[25] and juices of various plants [26] and hyperemia produced artificially [27] are among the many local treatments reported successful in small and uncontrolled groups. One large group of over 1,500 patients, entirely without a control, was treated by administering small doses of a complex mixture of various mineral salts three times a day for two months. If the warts (type unspecified) had not then disappeared the patient was instructed to wait two months and then to repeat the course. No statement of the average number of such courses necessary is made, but the report claims

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the Pathogenesis of These Lesions, J. Bone & Joint Surg. **7**:883 (Oct.) 1925. (*j*) Michael, J. C.: Roentgen-Ray Treatment of Verruca Plantaris, Arch. Dermat. & Syph. **13**:658 (May) 1926. (*k*) Montgomery, D. W., and Culver, G. D.: Verruca of the Nail Fold, ibid. **10**:425 (Oct.) 1924. (*l*) Nancel-Rénard, N.: Note sur le traitement des verrues plantaires par la radio-thérapie, Bull. Soc. franç. de dermat et syph. **28**:281 (May 18) 1921. (*m*) Osborne, E. D., and Putnam, E. D.: The Treatment of Warts, Radiol. **16**:340 (March) 1931. (*n*) Sisk, J. N.: Verruca Plantaris, ibid. **15**:564 (Nov.) 1930. (*o*) Taussig, L. R., and Miller, H. E.: Roentgen-Ray and Radium Treatment of Verruca Plantaris, Am. J. Roentgenol. **20**:514 (Dec.) 1928. (*p*) Young, W. J.: Verruca Vulgaris Treated with Radium: Case Report, Urol. & Cutan. Rev. **26**:31 (Jan.) 1922. (*q*) Zeisler, J.: Radiotherapeutic Observations, J. A. M. A. **40**:511 (Feb. 21) 1903.

22. Blanck: Eine einfache Methode Warzen schmerzlos und ohne erhebliche Narbenbildung zu entfernen, Deutsche med. Wchnschr. **49**:855 (June 29) 1923. Blendermann, L.: Eine einfache Methode Warzen schmerzlos und ohne erhebliche Narbenbildung zu entfernen, ibid. **49**:650 (May 18) 1923. Laemmle, K.: Eine einfache Methode Warzen ohne erhebliche Narbenbildung zu entfernen, ibid. **49**:885 (July 6) 1923.

23. Kren, O.: Ueber die Anwendung des Kohlensäureschnees in der Kosmetik, Wien. klin. Wchnschr. **40**:1329 (Oct. 20) 1927. Sutton, R. L.: The Treatment of Verruca Plantaris, J. Cutan. Dis. **27**:155 (April) 1909. Sutton, R. L.: A Clinical Note on Verrucae Plantares, Am. J. M. Sc. **144**:71 (July) 1912.

24. Gram, C.: Ueber die Behandlung von Warzen mit Calciumsalzen, Klin. Wchnschr. **6**:2069 (Oct. 22) 1927.

25. Maigre, E.: Action du bisulfite de soude sur les verrues et sur les condylomes, Compt. rend. Soc. de biol. **94**:118 (Jan. 22) 1926.

26. Hissard.: Les herbes aux verrues, Bull. Soc. franç. de dermat. et syph. **34**:695 (July) 1927. Michon, P.: Herbes aux verrues, ibid. **34**:36 (Feb.) 1927.

27. Ritter, C.: Zur Entstehung und Behandlung der Warzen, Berl. klin. Wchnschr. **58**:439 (May 2) 1921.

about 90 per cent cures.[28] The lack of control is typical of most of the reports in the literature on this subject.

Various preparations of arsenic by mouth have been used for some time in treating warts, but more important is the use of the arsphenamines. In 1910, Loeb[29] reported the disappearance of flat warts following one injection of arsphenamine, given for syphilis. Sutton,[30] in 1926, likewise noticed that after one month of antisyphilitic treatment with sulpharsphenamine, a patient lost flat warts of the face. He used one injection of 0.4 Gm. intramuscularly in 5 other cases "with satisfactory results." There is one report of a series of 45 patients treated by sulpharsphenamine (up to five injections) with about 50 per cent cures.[21m] Siemens[31] reported poorly controlled observations on the effect of injecting neoarsphenamine directly into common warts. A case of verruca vulgaris treated by neoarsphenamine injected intravenously with success[32] and the successful use of arsenic for 3 cases of condyloma acuminatum[33] have also been reported.

White, in 1915, was the first to use mercury in the treatment of flat warts. In all, he reported 10 cases, with 9 successes.[34] In most instances protiodide was used. Other investigators reported a total of about 40 cases of verruca plana juvenilis with similar treatment with from 40 to 80 per cent cures in from one week to one month.[35] No controlled cases were reported, and no allowance was made for spontaneous disappearance. It must be concluded that on the whole there is little evidence for the effectiveness of arsenic and mercury.

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28. Guyot: Note pour servir à l'étude des verrues, Lyon méd. **142**:469 (Oct. 21) 1928.

29. Loeb, H.: Erfahrungen mit Ehrlichs Dioxy-diamido-arsenobenzol (606), München. med. Wchnschr. **57**:1580 (July 26) 1910.

30. Sutton, R. L.: Sulpharsphenamine in the Treatment of Warts, J. A. M. A. **87**:1127 (Oct. 2) 1926.

31. Siemens, H. W.: Ueber die Wirkung des Salvarsans auf Warzen (Heilung durch intradermale Salvarsaninjektion), Arch. f. Dermat. u. Syph. **139**:113, 1922.

32. Lindsay, H. C. L.: Treatment of Common Warts by Neoarsphenamine, Arch. Dermat. & Syph. **10**:471 (Oct.) 1924.

33. Cedercreutz, A.: Zur internen Therapie der spitzen Kondylomen, Dermat. Centralbl. **10**:226 (May) 1907.

34. White, C. J.: The Use of Mercury in Verrucae Planae Juveniles, J. Cutan. Dis. **33**:738 (Nov.) 1915; The Use of Mercury in Verrucae Plane Juveniles, ibid. **34**:361 (May) 1916.

35. Fox, H.: The Treatment of Flat Warts by the Internal Administration of Mercury, Am. J. Dis. Child. **25**:55 (Jan.) 1923. Jadassohn, J.: Ueber die Behandlung von Verrucae planae juveniles mit Hydrargyrum iodatum flavum, Cor.-Bl. f. Schweiz. Aerzte **47**:1768 (Dec. 22) 1917. Ziegler, A.: Ueber die Quecksilberbehandlung von Warzen (und spitzen Kondylomen), München. med. Wchnschr. **68**:332 (March 18) 1921.

More recently Lurie [36] reported the use of bismuth salicylate intramuscularly for plantar warts. Of 49 patients treated, 34 were followed up, and all were cured. The usual number of injections was from one to three; the maximum (in 1 case only) was nine. The dose per injection was 2 grains (0.13 Gm.), smaller doses being used for children below 13 years. Here again the series was uncontrolled.

In contrast to the heavy metals are nonspecific agents. Grumach [37] introduced from 0.5 to 1 cc. of physiologic solution of sodium chloride intramuscularly in the upper part of the arm, the patients being told that they had been given a wonderful new specific remedy and that they would experience a burning or a feeling of heaviness in the parts bearing warts. Sixteen patients with verruca plana juvenilis of a total of 18 treated were cured in from one to four months. In a few cases distilled water was used with equal success. The author attributed the effectiveness of this treatment to suggestion. Dietel [38] reported over 80 per cent cures in treating 24 patients with verruca plana juvenilis by injecting sterilized fresh cow's milk intracutaneously, from two to four injections of 0.1 cc. each being given twice a week. In some cases the condition cleared up after three or four treatments; others required twenty or more before improvement started. Common warts and condylomas were not affected by this treatment. Here again there was practically no control. Although the author stated that the intracutaneous injection of nonprotein substances produced no results, he did not state how many cases were used as controls or how long the control treatment was persisted in. Moreover, no allowance is made for spontaneous cures. Duprat [39] reported success in treating 2 patients with verruca plana juvenilis by the intramuscular injection of 2 cc. of sterile milk, one dose a week, a total of two or three doses being necessary for cure. Sézary [40] reported 4 patients with verruca vulgaris and verruca plana juvenilis treated with more or less success by autohemotherapy. However, only 1 of the 4 was completely cured when last seen.

Such obvious confusion in the field of therapy led us to treat a small series of patients with bismuth intramuscularly and a control series with physiologic solution of sodium chloride intramuscularly, under exactly identical conditions, with the one exception that there was a

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36. Lurie, S.; Verrucae Vulgares (Palmar and Plantar): Treatment by Intramuscular Injections of Bismuth Salicylate, Arch. Dermat. & Syph. **26**:95 (July) 1932.

37. Grumach, L.: Ueber Suggestivbehandlung von Warzen, München. Med. Wchnschr. **74**:1093 (July 1) 1927.

38. Dietel, F.: Die Behandlung der Verrucae planae juveniles mit intrakutanen Milchinjektionen, Deutsche med. Wchnschr. **54**:2101 (Dec. 14) 1928.

39. Duprat, H.: Traitement des verrues planes juveniles par les injections de lait, J. de méd. de Bordeaux **107**:551 (July 10) 1930.

40. Sézary, A.: Traitement des verrues par l'autohémothérapie, Bull. Soc. franç. de dermat. et syph. **35**:839 (Nov.) 1928.

TABLE 1.—*Results of Treatment of Plantar Warts with Physiologic Solution of Sodium Chloride*

Patient	Age	Number of Warts	Location	Duration	Number Treatments	Comment	Result
1. R. L.	15	1	Sole	8 mos.	5	No change; patient then given bismuth (table 2)	Unimproved
2. F.Mc.F.	17	1	Sole; 2 verrucae vulgares on hands	4 mos.	5	At third week plantar wart turned black and 1 verruca vulgaris gone; at 5 weeks all gone	Cured
3. L. G.	25	1	Metatarsal region of sole	3 mos.	3	No change; then had 10 local treatments from LMD without improvement; on return to clinic treated with radium	Unimproved
4. J. K.	10	2	Heel	1 year	6	Larger of the two fell out before end of fourth week; three weeks later remaining bit of second was picked out with curet without bleeding	Cured
5. J. L.	23	3	Heel; small verruca vulgaris thumb	One for 1 year; satellites for 2 weeks	6	Pain disappeared after first injection; large wart black at three weeks, loose at five weeks, gone at 6 weeks; satellites removed by curet without drawing blood	Cured
6. H. J.	16	Over 25	Metatarsal region of sole	1 year	5	At third week, warts black and purplish area appeared among them (subcutaneous hemorrhage?); all out at five weeks	Cured
7. G. M.	14	3	Metatarsal region of both feet	4 mos.	4	Pain on walking gone on fifth day; wart black at one week; one bit left at three weeks; all out at two months	Cured
8. C. J.	14	2	Sole of left foot, big toe of right foot	6 mos.	4	Painful, preventing exercise; at two weeks gone except bit of one on sole; all out at four and eight weeks	Cured

LMD means local or family physician.

TABLE 2.—*Results of Treatment of Plantar Warts with Bismuth*

Patient	Age	Number of Warts	Location	Duration	Number Treatments	Comment	Result
1. R. L.	15	1	Sole	8 mos.	8	No improvement; new satellite warts found at end of course; radium given later	Unimproved
2. M. S.	16	1	Metatarsal region	8 mos.	5	Slight improvement at 4 weeks; plantar wart gone at 2 months; small verrucae vulgares on thumb still present	Cured
3. B. T.	20	2	Metatarsal region of both feet	2 mos.	4	No improvement; warts still present one month after last treatment	Unimproved
4. H. M.	19	5	Plantar surface left big toe	?	2	No improvement; warts present one month after last treatment; patient was then applying silver nitrate	Unimproved
5. E. K.	14	Over 15	Soles of both feet	2 mos.	7	No definite improvement until one week after sixth treatment; all gone one month later	Cured
6. H. G.	16	20	Sole	2 mos.	6	At one week all warts had turned black; second week several plantar warts gone and one of two verrucae vulgares had disappeared; 4 weeks all plantar warts gone; seventh week last verruca vulgaris disappeared	Cured
7. J. S.	18	1	Metatarsal region	1 mo.	7	Given seven weekly injections with no change; then sent for treatment with radium	Unimproved

charge of twenty-five cents for the bismuth and none for the physiologic solution of sodium chloride. All the patients were given a number in the order of their arrival at the clinic; the odd numbered patients were given bismuth and the even numbered physiologic solution of sodium chloride. It was possible to follow for a reasonable length of time 8 patients with plantar warts treated with physiologic solution of sodium chloride (2 cc. intramuscularly once a week) and 7 with plantar warts treated with bismuth (from 1 to 2 cc. of bismuth salicylate in oil intramuscularly once a week). Details are given in tables 1 and 2. Six of the 8 treated with physiologic solution of sodium chloride were cured of their plantar warts (75 per cent), while 3 of the 7 treated with bismuth were cured (about 45 per cent). The effect of both bismuth and physiologic solution of sodium chloride on verruca vulgaris was so slight in the few cases we observed that no details of these need be given. A further report on this aspect of the problem will be made from this clinic by Dr. E. L. Oliver and Dr. John Adams. We feel justified in drawing only one conclusion from this small series, but it is an important one, namely, that physiologic solution of sodium chloride is as effective as bismuth and no doubt as effective as any other preparation of heavy metal proposed as a specific for warts.

The mechanism of this cure of plantar warts, usually considered difficult to treat except with radium or roentgen rays, is not apparent. There are several possibilities: (1) that the warts would have disappeared spontaneously without treatment; (2) that the trauma of intramuscular injection, by destroying a certain small amount of tissue, may act as a nonspecific agent, and, (3) that the cure is by suggestion alone, the nature of the substance injected being irrelevant.

We have not demonstrated that the first possibility—spontaneous disappearance—can be discarded. Nevertheless, it was striking to see how in certain of the cases (as in cases 5 and 6, table 1) the warts turned black (the blood vessels had thrombosed) or the pain disappeared promptly after beginning treatment. The second possibility merits further investigation. Will the mere introduction of a needle without the injection of physiologic solution of sodium chloride accomplish as much? The third possibility—suggestion—must be discussed more fully because of the numerous reports of success with treatment by suggestion.

Bonjour wrote several papers [41] supporting the thesis that warts may be cured by, and even produced by, suggestion.. His work is charac-

41. Bonjour, J.: (*a*) L'influence de l'esprit sur le corps: A propos des verrues, Presse méd. **31**:1169 (July 14) 1923; (*b*) A propos des verrues, Schweiz. med. Wchnschr. **54**:748 (Aug. 14) 1924; (*c*) La guérison des condylomes par la suggestion, Presse méd. **36**:61 (Jan. 14) 1928; (*d*) Influence of the Mind on the Skin, Brit. J. Dermat. **41**:324 (Aug.-Sept.) 1929; (*e*) Théorie psycho-vasomotrice des verrues et des condylomes acuminés, Ann. de. dermat. et syph. **1**:209 (Feb.) 1930; (*f*) footnote 19.

terized, however, by an entire lack of figures or controls. He worked out an explanation of his cure, claiming to demonstrate lowering of the diastolic blood pressure and slowing of the pulse when atrophy of the warts begins. Changes in blood pressure are from 1 to 2 cm. of mercury. He supported this finding by reporting that in several thousand cases of psychoneurosis (phobias, tic, etc.) he found a similar elevation of the diastolic pressure, warts thus being produced by psychoneurosis. The success of all experiments in transmission was then explained on this basis: No specific virus is present, and suggestion alone produces the wart. It is rather difficult to reconcile with this theory the appearance of warts in dogs and cattle. It is also difficult to understand why in children a tuberculin test or similar intracutaneous inoculation should not often produce a wart, especially if the child already has warts. Such an occurrence has not been reported.

Bonjour's methods, including his "absent treatment," are best described in his own words:[41b]

> This is how I proceed in the majority of cases in order to produce the improvement and the cure: The patient puts his hand on a sheet of paper; I run a pencil around the fingers, then draw the warts in full size. Then I cover the patient's eyes with a triple thickness of cloth to prevent his seeing. I make him hold out his hands; lightly I touch his warts with my fingers or a glass rod and I say: "From this day on you will never again feel any warts and they will disappear; do not touch them again . . . ."
>
> Sometimes, in a social gathering, the subject is brought up, and someone will say to me: "I have a wart; make it disappear, for no one has ever been able to cure it. It always comes back." In all such cases, I simply reply: "Never think of it again and you will be cured." I do nothing else and I don't know a single case of failure.
>
> These facts demonstrate that it is sufficient to promise the cure to produce it . . . .
>
> Finally, . . . you don't have to see the patient. On Sept. 30, 1902, I replied to a young lady . . . who wrote me on the subject of her warts: "Draw a picture of your hands; mark on the sketch the outline of the warts, and don't bother with them any more. On November 1, you will send me the sheets of paper, telling me that all the growths have disappeared." On November 1, she sent me the sketches, announcing the cure.

In addition, Bonjour expressed the belief that he could cure eczema by suggestion and, by producing a mild state of hypnosis, also erythroderma, hyperhidrosis, urticaria, hay fever and asthma. He also experimented with the initiation of labor by suggestion.

Bloch,[42] in contrast to Bonjour, produced figures on the treatment of verrucae by suggestion. Of 228 patients treated, 179 were followed up by letter or by visit. Of these, 98 (54.5 per cent) were cured; of the 98 cured, 43 per cent were cured in the first, 39 per cent in the

42. Bloch, B.: Ueber die Heilung der Warzen durch Suggestion, Klin. Wchnschr. **6**:2271 (Nov. 26); **6**:2320 (Dec. 3) 1927.

second and 18 per cent in the third month. Of 136 cases of verruca vulgaris 44.1 per cent were cured; of 43 cases of verruca plana juvenilis, 88.4 per cent were cured. Bloch's method included blindfolding the patient, turning on an electric motor, painting the warts with a dye and warning the patient not to touch them until the color disappeared. Various common laboratory dyes were used. Bloch concluded that the stronger the emotional response on the part of the patient the better the chance of effecting a cure. As he pointed out, the percentage of success is as high as by any other method. This may be interpreted as an indication of the inefficacy of all treatment.

An attempt to answer the objection to these figures on the ground of a lack of control was made by Memmesheimer and Eisenlohr.[7] These investigators went to a small town in Wurtemberg, saw school children, factory workers and patients in clinics (with irrelevant complaints) and noted the addresses of all who had warts. In all, 140 cases were found. Seventy patients so chosen that they would not come in contact with the other 70 were given treatment by suggestion, according to Bloch's method. The other 70 were given no treatment. The patients were then seen one-half, one, three and six months later. At the end of that time 17 of those treated were free from warts, whereas 20 of those given no treatment had lost their warts spontaneously. The time elapsed before disappearance of the warts was shorter, on the average, for those treated than for those untreated, but since so few cases are involved this cannot be accepted as evidence of the effectiveness of suggestion. If anything, it throws doubt on the effectiveness of suggestion, but a definite answer must await the investigation of a larger number of cases in regard to spontaneous disappearance.

There remains for consideration Biberstein's treatment of warts by immunotherapy.[43] He prepared a vaccine from warts and condylomas, of which he injected 0.1 cc. intracutaneously twice a week. From one to five injections gave no results, from five to ten gave 50 per cent cures and from ten to twenty gave 75 per cent cures. In a later paper,[43b] he reported about 65 per cent success with verruca vulgaris and about 85 per cent success with both verruca plana juvenilis and condyloma acuminatum. With extracts of normal skin he had only from 20 to 30 per cent cures. A vaccine was also prepared from bovine warts and was used on human subjects with the following results:

	Number Treated	Number Cured	Per Cent
Verruca vulgaris	23	13	56.5
Verruca plana juvenilis	7	7	100.0
Condyloma acuminatum	10	9	90.0

43. Biberstein, H.: Versuche über Immuntherapie der Warzen und Kondylomen, Klin. Wchnschr. **4**:638 (April 2) 1925; (*b*) Die Immuntherapie der Warzen und Kondylomen, ibid. **11**:1021 (June 11) 1932.

Larger doses were injected when bovine warts were used as a source, and injection was subcutaneous instead of intracutaneous. It is interesting to note that 23 calves were treated with the bovine extract, and all were cured after about four injections, only a few requiring more. Each dose was from 5 to 10 cc., administered subcutaneously. However, control injections of a vaccine prepared from normal calf skin or of 0.5 per cent phenol in physiologic solution of sodium chloride also cured all calves to which it was given, the number of calves so treated not being stated. Like Bloch, Biberstein found verruca plana juvenilis easier to treat than verruca vulgaris. With the latter his success is considerably better than Bloch's. The work needs confirmation by other investigators, as well as controls to determine the part played by spontaneous disappearance.

In conclusion, the following are the more important topics which await fuller investigation: (1) the natural history of the untreated wart; (2) the virus, for which suitable methods of transfer, suitable animals and means of concentration are to be discovered; (3) therapy, which must be under rigid control, and (4) immunology, which must eventually explain why some are susceptible to warts while others are not, and why spontaneous disappearance occurs.

SUMMARY

Warts occur in man, cattle, dogs and horses. Verruca vulgaris, the filiform wart, verruca plana juvenilis and condyloma acuminatum are related, possibly being caused by the same virus. There is no experimental evidence for or against the relationship of the plantar wart to the others in the group. These lesions are contagious and are caused by a filtrable virus about which little is known except that it is filtrable. An unsuccessful attempt to produce encephalitis with this virus is reported. The many treatments proposed are discussed, and the conclusion is reached that they are of doubtful value, since almost all the experiments have been entirely uncontrolled. To demonstrate the necessity for control a report is made of 8 cases of plantar warts in which physiologic solution of sodium chloride was given intramuscularly and 6 in which bismuth was given intramuscularly with approximately equal therapeutic effectiveness. Suggestion, which may play a part in these results, will be difficult to evaluate properly until more is known of the natural history of warts. Specific therapy in the hands of Biberstein presents the same difficulty in evaluation, but merits further investigation and confirmation by other workers.

ARSPHENAMINE DERMATITIS

ATTEMPTED SENSITIZATION TO NEOARSPHENAMINE AND FURTHER OBSERVATIONS ON THE PATCH TEST

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Three years ago I published the results of the patch test in eight cases of postarsphenamine dermatitis. The conclusion of that study was that a positive patch test was an absolute contraindication to further arsphenamine therapy, but that a negative patch test permitted further administration of the arsphenamines. A résumé of the literature accompanied the communication.[1]

At that time it was thought that the patch test probably was the best method of determining cutaneous sensitization to the arsphenamines. The scratch test was thought to be unreliable, and the intradermal test was regarded as a procedure which might produce sensitivity to the drug. Moore, Woo, Robinson and Gay[2] studied the intradermal test in different types of patients. Their results showed positive reactions in 60 per cent of normal persons, in 70 per cent of patients who had had arsphenamine dermatitis and in 94 per cent of patients with hay fever. Cannon and Karelitz[3] studied the intradermal test and concluded that the number of positive reactions (48.7 per cent) was not high enough for practical purposes. They further concluded that the test was lacking in specificity and had no diagnostic value. In a recent communication Robinson[4] reported the results of studies of the patch test and concluded that the positive test was confirmatory evidence of the persistence of sensitization, but that the test was of no practical value, since it was sometimes positive in normal persons and often negative

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Read before the Section on Dermatology and Syphilology at the Eighty-Fifth Annual Session of the American Medical Association, Milwaukee, June 15, 1933.

1. Schoch, A. G.: The Patch Test and the Element of Syringe Contamination in Arsphenamine Dermatitis, J. A. M. A. **98**:1367 (April 16) 1932.

2. Moore, J. E.; Woo, S. T.; Robinson, H. M., and Gay, L. N.: Reactions of the Skin Following the Intradermal Injection of Arsphenamine: Postarsphenamine Dermatitis, Arch. Dermat. & Syph. **23**:74 (Jan.) 1931.

3. Cannon, A. B., and Karelitz, M. B.: Intradermal Tests in Relation to Arsphenamine Dermatitis: A Study of Two Hundred and Fifty-Six Clinical Cases, Arch. Dermat. & Syph. **29**:485 (April) 1934.

4. Robinson, H. M.: The Importance of Patch Tests in Determination of Arsphenamine Sensitization, South. M. J., to be published.

in patients known to be sensitive to the arsphenamines. Beerman [5] reported that routine patch testing resulted in an increased incidence of arsphenamine dermatitis in Stokes' clinic.

In the past three years I have done patch tests on seventeen patients who had manifested cutaneous intolerance to the arsphenamines (see table). Fourteen of the seventeen patients presented examples of the

Patch Tests in Fourteen Patients with Cutaneous Intolerance to Arsphenamine

Patient, Age	Race, Sex	Diagnosis	No. Injections	Drug	Duration of Dermatitis, Weeks	Infiltration	Positive Patch Test Within	
N. M. O. 19	W F	Late secondary syphilis	8 (0.6 Gm.)	Neoarsphenamine	3	No	4 months	Dextrose administered intravenously
A. P. 25	W F	Late tertiary syphilis of the bone	5 (0.6 Gm.)	Neoarsphenamine	5	No	3 months	Nephritis; boils
H. B. 27	W F	Late secondary syphilis	4 (0.6 Gm.)	Neoarsphenamine	4	Yes	2 months	Nephritis
B. K. 28	W F	Late secondary syphilis	7 (0.6 Gm.)	Neoarsphenamine	7	Yes	2 months and 2 years	
J. O. 20	W F	Late latent syphilis	9 (0.6 Gm.)	Neoarsphenamine	4	No	2 months	Recurred after 0.16 Gm. neoarsphenamine
T. S. 40	W M	Tabes	18 (0.6 Gm.)	Neoarsphenamine	8	No	6 years	Generalized itching
I. B. 25	W F	Late latent syphilis	6 (0.6 Gm.)	Neoarsphenamine	4	Yes	4 months	
J. F. W. 52	W M	Aneurysm	3 (0.2 Gm.)	Bismarsen	7	....	5 months	Tolerant to bismuth
J. C. 35	C M	Late latent syphilis	8 (0.6 Gm.)	Neoarsphenamine	4	No	2 months	
L. H. 26	W F	Late latent syphilis	16 (0.6 Gm.)	Neoarsphenamine	4	No	3 months	
A. McG. 35	C M	Late latent syphilis	3 (0.6 Gm.)	Neoarsphenamine	9 mos.	No	10 months	Generalized papular eruption
G. M. 68	W M	Tabes	11 (0.6 Gm.)	Neoarsphenamine	6	Yes	1 year	
M. M. 26	W M	Late latent syphilis	9 (0.6 Gm.)	Neoarsphenamine	6	No	3 months	
I. W. 23	W F	Late latent syphilis	7 (0.6 Gm.)	Neoarsphenamine	6	No	1 year	Generalized itching

exfoliative type of arsphenamine dermatitis which I believe to be of the allergic type. In all fourteen of these patients the patch test was strongly positive. In most cases the test was strongly positive on repeated examination. One patient gave a persistently positive reaction six years after the development of the dermatitis. In the remaining three of the seventeen patients, one gave a history of having had a "rash" following an injection of neoarsphenamine; the patch test was weakly positive, and 0.1 Gm. of bismarsen produced an urticarial eruption of

5. Beerman, H.: Cutaneous Sensitization to Arsenic Through the Patch Test, Arch. Dermat. & Syph. **28**:296 (Aug.) 1933.

three days' duration. Erythema multiforme and foot drop developed in the second patient following eleven injections of neoarsphenamine. After the skin had returned to normal, the patch test gave negative results. A year later the patient received three injections of neoarsphenamine which precipitated an exudative dermatitis. The patch test was repeated six months later, and it was strongly positive. A generalized papular dermatitis, thought to be a toxic arsphenamine eruption, developed in the third patient. After recovery, the reaction to the patch test was weakly positive. This patient subsequently tolerated eighteen injections of bismarsen, after which the drug was stopped because of the reappearance of a similar eruption.

Since the patch test is of value only in determining epidermal sensitivity, it is not surprising that the results of the patch test in the three patients just mentioned were as reported. Urticaria and erythema multiforme are preponderantly vascular reactions and involve the epidermis only secondarily. The patch test probably serves only as a means of detecting extreme epidermal hypersensitiveness to the arsphenamines, such as is present for a varying length of time following the attack of exfoliative postarsphenamine dermatitis. It is this type of arsphenamine eruption that is probably best explained on an allergic basis. It is this type of eruption that carries the high mortality rate.

It has previously been thought by observers such as Klauder, Frei, Nathan and Grundmann, Sulzberger and myself that intradermal injections of neoarsphenamine in man and animals are capable at times of sensitizing the organism. Frei [6] sensitized 12 per cent of nonsyphilitic patients. Sensitivity was determined by subsequent intradermal tests progressing from negative to positive. Frei's work was confirmed by Nathan and Grundmann.[7] Sulzberger,[8] experimenting with guinea-pigs in Breslau, seemed to confirm these observations. He failed to verify his results when the experiments were repeated in New York. Clinical and experimental results such as these have led many observers to feel, therefore, that accidental extravasation of neoarsphenamine into and under the skin was conducive to the development of sensitization. Arsphenamine dermatitis sometimes follows paravenous injections; often

6. Frei, W.: Ueber willkürliche Sensibilisierung gegen chemischdefinierte Substanzen: I. Untersuchungen mit Neosalvarsan am Menschen, Klin. Wchnschr. **7**:539 (March 18) 1928; II. Untersuchungen mit Neosalvarsan am Tier, ibid. **7**:1026 (May 27) 1928.

7. Nathan, E., and Grundmann, H.: Chemische Analyse der Hautüberempfindlichkeit nach experimenteller Sensibilisierung mit Salvarsan, Dermat. Ztschr. **59**:367 (Nov.) 1930.

8. Sulzberger, M. B.: Arsphenamine Hypersensitiveness in Guinea-Pigs: II. Experiments Demonstrating the Rôle of the Skin, Both as Originator and as Site of the Hypersensitiveness, Arch. Dermat. & Syph. **22**:839 (Nov.) 1930.

it does not. In the last two years I have seriously doubted whether this mechanism played a prominent rôle in the development of arsphenamine dermatitis. In only four of the seventeen cases reported in this series was there a history of accidental extravasation previous to the development of arsphenamine dermatitis.

In an attempt to verify or disprove this fact the following experiment was undertaken: In the clinic for syphilitic diseases at the City-County Hospital, approximately one half of the new patients received 0.2 cc. of a 1 per cent solution of neoarsphenamine intradermally before antisyphilitic treatment was instituted. The total number of patients receiving the intradermal injection was one hundred and eighty-six. One hundred and forty-six of these had never previously received any arsphenamine. Of the one hundred and forty-six, forty-five were immediately started on the first course of neoarsphenamine. The remaining one hundred and one patients were given a course of bismuth salicylate in oil consisting of from five to ten weekly injections before neoarsphenamine was administered. At the time of the present writing all of the patients have received one or more courses of neoarsphenamine. *Not one patient developed arsphenamine dermatitis.* In none of the patients has treatment been interrupted because of the appearance of suspected beginning arsphenamine dermatitis. In a similar treated group of patients who received no "sensitizing dose" one patient had arsphenamine dermatitis. The treatment was interrupted in two others because of suspected impending arsphenamine dermatitis.

Although this experiment does not prove that an intradermal injection of neoarsphenamine solution is not a factor in the production of arsphenamine dermatitis, it strongly suggests that such intradermal injections do not play a major rôle in its development. Certainly one cannot say that 12 per cent of patients who have never received previous arsphenamine treatment become sensitized after an intradermal injection of neoarsphenamine solution.

SUMMARY AND CONCLUSIONS

1. A strongly positive patch test performed with neoarsphenamine solution is indicative of extreme epidermal hypersensitiveness to the drug and should be an absolute contraindication to the further use of the arsphenamines even in minute doses.

2. A negative patch test should precede a resumption of arsphenamine therapy in a patient who has recovered from arsphenamine dermatitis.

3. That intradermal injections of small amounts of neoarsphenamine solution or the accidental infiltration of the tissue by paravenous injections does not materially increase the risk of development of arsphenamine dermatitis in the treatment of syphilis is shown.

VALUE OF ORGANIC LUETIN IN DIAGNOSIS AND TREATMENT OF SYPHILIS

A STUDY OF NINE HUNDRED CASES

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During the past few years there has been a renewed interest in organic luetin in relation to the cutaneous reactions to its injection in syphilis. Several writers have given encouraging reports, the most optimistic of which have come from abroad.

Noguchi,[1] in 1911, using a luetin prepared from an extract of killed ascites agar cultures of Spirochaeta pallida, found that the skin of untreated patients with primary and secondary syphilis reacted negatively, while 70 per cent of those who had received arsphenamine gave positive reactions. In cases of congenital and late syphilis, almost 100 per cent of the patients gave positive reactions. The luetin reaction often remained positive after the Wassermann reaction of the blood became negative.

Cohen,[2] Ziegel,[3] Wolfsohn,[4] Pusey,[5] Brown[6] and others reported almost equally good results with Noguchi's luetin.

The culture luetin continued to have many supporters until Clausz,[7] Sherrick,[8] Cole and Paryzek[9] called attention to the fact that a positive

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The luetin was prepared and furnished by Dr. George Raiziss and Dr. M. Severac.

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Organic luetin has not been accepted by the Council on Pharmacy and Chemistry of the American Medical Association. For the report on this product see The Journal of the American Medical Association (**101**:929 [Sept. 16] 1933).

1. Noguchi, H.: J. Exper. Med. **14**:557 (Dec.) 1911.

2. Cohen, M.: Arch. f. Ophth. **41**:8, 1912.

3. Ziegel, H. F. L.: The Practical Value of Noguchi's Luetin Reaction, Arch. Int. Med. **9**:520 (April) 1912.

4. Wolfsohn, J. M.: The Cutaneous Reaction in Syphilis, J. A. M. A. **60**:1855 (June 14) 1913.

5. Pusey, W. A.: Am. J. M. Sc. **146**:504, 1913.

6. Brown, A.: The Luetin Reaction in Infancy, Am. J. Dis. Child. **6**:171 (Sept.) 1913.

7. Clausz, M.: München. med. Wchnschr. **61**:1933, 1914.

8. Sherrick, J. S.: The Effect of Potassium Iodide on the Luetin Reaction, J. A. M. A. **65**:404 (July 31) 1915.

9. Cole, H. H., and Paryzek, H. V.: The Provocation of the Luetin Test in Nonsyphilitic Patients, J. A. M. A. **68**:1089 (April 14) 1917.

reaction could be obtained even in nonsyphilitic patients who were taking iodide or bromide medication. It was also pointed out by Stokes [10] and others that certain sterile substances such as agar, starch and skin emulsions, when injected intracutaneously would produce a reaction similar to that of culture luetin.

Attention was then turned to the various organ luetin preparations which would possibly have a more specific reaction than Noguchi's culture luetin. Various syphilitic organ extracts were used, such as liver, spleen, kidney, pneumonia alba, lymph nodes and acute syphilomas of rabbit's testicles, an extract of the last-mentioned substance being marketed in Vienna under the name of luotest.[11]

Lehner and Rajka,[12] using Busson's [13] liver luetin, found that 38 per cent of 278 syphilitic patients gave a positive reaction, and 50 per cent of the patients with a positive reaction had a negative Wassermann reaction of the blood.

Hollander,[14] working with Busson's luetin, stated that a positive reaction was found in from 80 to 90 per cent of patients with gummas of the skin, mucous membrane and the periosteum and bone, and in 45 per cent of persons with superficial lesions. He also found that 85 per cent of persons with congenital syphilis and 95 per cent with interstitial keratitis gave a positive reaction. Negative results were obtained in cases of primary syphilis and in most cases of secondary syphilis; also in cases of tabes dorsalis and dementia paralytica. In this work, however, Hollander did not use a control solution.

Kolmer,[15] in 1930, using a saline suspension of acute syphilitic testes of rabbits, obtained 33 per cent positive reactions in 159 cases of acquired syphilis in which the Wassermann reaction was positive, and in 61 per cent of 33 cases of congenital syphilis.

Planner,[16] using luotest, found that 80 per cent of patients with tertiary syphilis gave a positive reaction to the luetin test, while Müller and Stein obtained 87 per cent positive reactions in the tertiary group. Planner further stated that the factors restricting the Noguchi luetin, namely, provocation of the reaction by iodides and bromides, did not apply to the organ extracts. He regarded luotest as a specific.

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10. Stokes, J. H.: A Luetin Reaction in Syphilis Produced by Agar, J. A. M. A. **68**:1092 (April 14) 1917; J. Cutan. Dis. **32**:560, 1914.

11. This product has not been accepted by the Council on Pharmacy and Chemistry of the American Medical Association.

12. Lehner, E., and Rajka, E.: Dermat. Wchnschr. **84**:502 (April 9) 1923.

13. Busson, B.: Wien. klin. Wchnschr. **37**:333 (April 3) 1924.

14. Hollander, L.: Organic Luetin: Its Use in the Diagnosis of Syphilis, Arch. Dermat. & Syph. **17**:797 (June) 1928.

15. Kolmer, J. A., and Tuft, L.: Chemotherapy **8**:10 (April) 1931; Am. J. Syph. **14**:241 (April) 1930.

16. Planner, H. J.: Chemotherapy **8**:15 (April) 1931.

Gandy,[17] working with the Kolmer luetin, tested 200 syphilitic patients and found that 10 per cent of those with primary and secondary lesions gave positive reactions, while 34 per cent of those with latent syphilis, 28 per cent of those with cerebrospinal syphilis, 11 per cent of those with cardiovascular syphilis and 31 per cent of those with congenital syphilis gave positive reactions. He also found that the luetin reaction, in many cases, remained positive after the serum became negative.

Fessler[18] said that the cutaneous reactions to luotest were always positive in the deeper forms of tertiary syphilis and almost always positive in the superficial forms. Other stages of syphilis varied with the duration of the disease and the amount of treatment received, the reaction to the luetin test often remaining positive after the serum had become negative.

Ciarrocchi,[19] in 1932, using luotest, found that patients with primary and secondary syphilis, tabes dorsalis and dementia paralytica gave negative reactions. Seventy-seven per cent of persons with gummas and 26 per cent of those with latent syphilis gave positive reactions, while 4 persons with interstitial keratitis gave positive reactions.

Ambler,[20] in 1933, using Kolmer organic luetin, obtained positive results in the following cases: latent syphilis, 12.5 per cent; early active syphilis, 8.3 per cent; late active syphilis, 24.7 per cent; syphilitic aortitis and aneurysm, 11.1 per cent; gummas of the skin, 100 per cent; congenital syphilis, 87.5 per cent, and interstitial keratitis and iridocyclitis, 100 per cent. He also stated that the administration of iodides and bromides to nonsyphilitic patients did not provoke a true positive luetin reaction but, instead, it produced pseudoreactions. He concluded, however, that organic luetin was not of sufficient diagnostic value to warrant its general use.

The following report is submitted in an endeavor to evaluate the organic luetin reaction and its therapeutic application.

PROCEDURE

The Kolmer luetin test was performed on patients, in a routine manner, as they presented themselves at the Vanderbilt Clinic, New York City Hospital and St. Luke's Hospital Clinic. They comprised

17. Gandy, D. T.: The Interpretation of the Dermoluetin Reaction in Syphilis: Experience with the Kolmer Organic Extract, Arch. Dermat. & Syph. **24**:937 (Dec.) 1931.

18. Fessler, A.: Arch. f. Dermat. u. Syph. **163**:271 (June) 1931.

19. Ciarrocchi, Luigi: Policlino (sez. med.) **39**:553 (Nov.) 1932.

20. Ambler, J. V.: Diagnostic Value of the Organic Luetin Reaction, Arch. Dermat. & Syph. **28**:353 (Sept.) 1933.

males and females of all ages and in all stages of syphilis, with and without treatment. Subsequently, new patients entering the Vanderbilt Clinic and the City Hospital were also tested. Only those not receiving potassium iodide were used for this report—a total of 627 patients.

TECHNIC

One tenth cubic centimeter of the luetin and the same quantity of the control solution were injected intracutaneously into the anterior surface of the forearm. The luetin was injected from 3 to 4 inches (7.6 to 10.16 cm.) below the control site. The tests were read at the end of forty-eight hours.

Positive reactions consisted of an area of bright erythema 10 mm. or more in diameter, or a red papule the size of a split pea surrounded by a red areola from 5 to 15 mm. in diameter at the site of the injection of the luetin. The reactions were negative, or practically so, at the site of the injection of the control solution.

The pseudoreactions, which were areas of erythema at the site of the injection of the luetin and of the control solution, were classed as negative.

In the report on results the cases have been subdivided into various groups according to the stage of syphilis they presented.

RESULTS

The first group included 110 cases of primary and secondary syphilis. All the patients had contracted the infection within a year. Some had received considerable treatment at the time the test was done.

Cases	Positive Luetin Reactions
Total group (110)	24.5%
81, with positive Wassermann reactions of the blood	25.0%
29, with negative Wassermann reactions of the blood	20.0%

The second group was comprised of 240 cases of so-called latent syphilis. Some of these patients had been under treatment for several years. All had positive Wassermann reactions of the blood at the beginning of treatment; some, however, had negative reactions at the time the test was done.

Cases	Positive Luetin Reactions
Total group (240)	38.0%
175, with positive Wassermann reactions of the blood	38.2%
65, with negative Wassermann reactions of the blood	37.0%

The third group consisted of 97 cases of cerebrospinal syphilis of all types.

Cases	Positive Luetin Reactions
Total group (97)	38.0%
79, with positive Wassermann reactions of the blood	40.0%
18, with negative Wassermann reactions of the blood	33.3%

The fourth group was made up of 40 cases of superficial and deep types of gummas. Some of the patients had received treatment at the time the test was made and, in a few instances, the lesions had disappeared clinically.

Cases	Positive Luetin Reactions
Total group (40)	77%
34, with positive Wassermann reactions of the blood	82%
6, with negative Wassermann reactions of the blood	50%

The fifth group was comprised of 23 cases of syphilitic aortitis and aneurysm. Some of the patients had a positive Wassermann reaction of the spinal fluid.

Cases	Positive Luetin Reactions
Total group (23)	48%
18, with positive Wassermann reactions of the blood	50%
5 with negative Wassermann reactions of the blood	40%

In the sixth group were 117 cases of congenital syphilis. Most of the patients were receiving treatment.

Cases	Positive Luetin Reactions
Total group (117)	40.0%
67, with positive Wassermann reactions of the blood	43.0%
50, with negative Wassermann reactions of the blood	34.0%
Interstitial keratitis (16)	62.5%

There were also 26 babies and children born of syphilitic mothers, but with no stigmas of syphilis, and 7.5 per cent of these gave a positive luetin reaction. Twenty-one of the mothers were tested, and a positive luetin reaction was obtained in 5, of whom 2 were the mothers of the babies with positive luetin reactions.

In the seventh group were 227 nonsyphilitic patients from the medical wards of St. Luke's and City hospitals who were used as controls. Eight patients, or 3.5 per cent, gave positive luetin reactions, while an additional 9 gave pseudoreactions. One patient gave a negative reaction at the end of forty-eight hours, and herpes zoster developed over the left buttock one day later; at the same time, the site of the injection of luetin became red and tender and itched considerably. This delayed allergic reaction, unless produced by the herpes zoster, is difficult to explain.

It is interesting to note in the first six groups of patients what a high percentage of positive luetin reactions was obtained in patients with a negative Wassermann reaction. This is thought to be of prognostic significance in determining when a patient is cured of syphilis. It is more likely merely an expression of the fact that the two reactions

are based on entirely different phenomena, one on allergy and the other on the formation of antibodies; consequently, they do not follow the same course.

In order to determine the effect of treatment on the luetin reaction, the patients whose exact amount of treatment was known were tabulated in the following manner: (1) those who had received no treatment; (2) those who had received a little treatment (from one to ten injections of both arsphenamine and mercury, or the equivalent); (3) those who received a moderate amount of treatment (from eleven to twenty injections of both arsphenamine and mercury, or the equivalent), and those receiving intensive treatment (over twenty injections of both arsphenamine and mercury).

TABLE 1.—*Effect of Treatment on the Luetin Reaction*

Amount of Treatment	Secondary		Latent Syphilis		Cerebrospinal Syphilis		Gummas		Aortitis		Congenital Syphilis	
	Number of Cases	Per Cent Positive	Number of Cases	Per Cent Positive	Number of Cases	Per Cent Positive	Number of Cases	Per Cent Positive	Number of Cases	Per Cent Positive	Number of Cases	Per Cent Positive
None	53	20	14	42	12	50	16	87	4	75	4	100
Little	20	20	20	30	20	40	5	100	4	75	17	40
Moderate	43	20	43	39	11	45	6	100	4	50	33	37
Intensive	4	75	37	48	20	25	4	50	11	27	46	44

TABLE 2.—*Percentage of Positive Luetin Reactions in Relation to Sex*

	Secondary Syphilis	Latent Syphilis	Cerebrospinal Syphilis	Gummas	Aortitis	Congenital Syphilis
Male	22.5	35	41	78	54	41
Female	28.0	39	38	90	28	39

From an analysis of the data in table 1, it is seen that in the cases of cerebrospinal, gummatous and congenital syphilis and of aortitis, treatment reduced the number of positive luetin reactions. In the secondary and latent groups it had no influence on the reaction. Gandy and Ambler found in their series a higher percentage of positive reactions in the patients who had received intensive therapy, and described as a possible explanation the breaking down of syphilitic foci and the releasing of reacting bodies as a result of treatment.

Table 2 tabulates the percentage of positive luetin reactions in the various groups in their relation to sex. It is seen that in the secondary, gummatous and latent groups the incidence of positive reactions in females is higher, while in the groups with aortitis and cerebrospinal and congenital syphilis, the positive reactions in males predominate. Except, possibly, in aortitis, the figures are so nearly equal they indi-

cate that sex has no influence on the luetin reaction. Ambler found a much higher percentage of positive reactions in women than in men, a condition which he could not explain.

INFLUENCE OF IODIDES AND BROMIDES ON THE LUETIN REACTION

Eighty-four nonsyphilitic and 30 syphilitic patients with negative reactions to luetin were given potassium iodide, 10 grains (0.65 Gm.), three times a day, and again tested with both the luetin and the control solutions. Thirty-one per cent gave a marked positive reaction to the second test, and 33.5 per cent gave extensive pseudoreactions. Many of the latter were more marked at the site of the injection of the luetin than at the site of injection of the control solution. Only half as many pseudoreactions were noted in the syphilitic as in the nonsyphilitic patients, while the positive reactions were about equally divided. Most of the patients continued to give a positive reaction three weeks after the iodides had been discontinued.

In 12 of the patients headache, sore throat, nausea and suffusion of the eyes developed, and in 2 others a purpuric eruption of the extremities. These reactions were probably produced by the iodides, but it is of interest to note that the symptoms occurred in so many patients and that they gave either a positive luetin reaction or a pseudoreaction.

Fifty patients who reacted negatively to luetin were given sodium bromide orally, 5 grains (0.32 Gm.), three times a day, and again tested with organic luetin. Six patients gave positive reactions, and an additional 5 gave mild pseudoreactions. The reactions which could be classified as positive were not nearly so extensive as in the patients who received iodides.

With the various sources of obtaining iodides and bromides such as in tonics, sedative preparations, iodized salt and the use of iodides in the treatment of syphilis, one can understand the uncertainty of the luetin test when it is so influenced by these drugs.

COMPARATIVE VALUE OF VARIOUS ORGANIC LUETIN PREPARATIONS

In order to compare the value of various organic luetins, the following preparations were used:

1. Kolmer organic luetin. This is syphilomatous tissue of rabbit's testicles in a saline suspension and contains from 8 to 15 dead spirochetes per dark field. The nitrogen content is 4.59 mg. per hundred cubic centimeters. Control solutions are prepared in the same manner from normal testicular tissue. The nitrogen content is 4.78 mg. per hundred cubic centimeters.

2. Neurotropic organic luetin. This is prepared in the same manner as the Kolmer luetin, but neurotropic Spirochaeta pallida, as isolated by Raiziss and Severac,[21] is used. The nitrogen content is 4.01 mg. per hundred cubic centimeters.

3. Resistant organic luetin. The method of preparation is the same as for the Kolmer luetin, but a resistant strain of Spirochaeta pallida, as isolated by Dr. Raiziss, is used. The nitrogen content is 3.86 mg. per hundred cubic centimeters.

4. Luotest (Müller and Brandt). This is an extract of rabbit testicular syphilomas. The nitrogen content is 3.46 mg. per hundred cubic centimeters.

5. Busson luetin. This is an extract of congenital syphilitic liver tissue.

Two hundred syphilitic patients were tested with both Kolmer and neurotropic luetin and all but 4 gave the same positive results. In 3 of these, the neurotropic reaction was negative when the reaction to the Kolmer luetin was positive, and the opposite was true in a case of neurosyphilis.

One hundred and twelve syphilitic patients were tested with the Kolmer luetin, resistant-strain luetin and luotest. Forty-four gave positive reactions to the Kolmer and resistant-strain luetin, while 7 gave negative reactions to luotest. In 10 cases there was a smaller positive reaction to luotest than to the other preparations.

Twenty patients with positive reactions to the Kolmer luetin were tested with the Busson luetin, and only 14 reacted positively.

The results of these tests indicate that organic luetin prepared according to the Kolmer method gives a higher percentage of positive reactions than the extract preparations.

The identical results obtained with the three organic luetins prepared from different strains of Spirochaeta pallida indicate that there is no specific reaction to the various strains of these organisms.

RESULTS OF VACCINE TREATMENT OF SYPHILIS

Seven patients with syphilitic gummas were treated with biweekly injections of from 0.3 to 0.5 cc. of Kolmer organic luetin intracutaneously with the following results:

Healing of the lesions occurred in 1 case, improvement in general well-being, but no change in the local lesions, in a second case, and no improvement in the remaining 5 cases.

21. Raiziss, G. W., and Severac, Marie: Neurotropism of Spirochaeta Pallida: Experimental Studies with Special Reference to Asymptomatic Syphilis of Mice, Arch. Dermat. & Syph. **26**:271 (Aug.) 1932.

The patient in whom the lesions healed was an Irish-American, aged 69, who had three ulcerating gummas on the scalp and one on the forehead, varying in size from ½ to 1¾ inches (1.27 to 4.45 cm.) in diameter. They were oval with red, beveled edges and exposed the skull at the base. The Wassermann reaction of the blood was four plus. After the first injection, a marked inflammatory reaction developed in, and around, all the lesions, and in two weeks they were entirely healed except for a slight central crusting on the lesion on the forehead. Two weeks later, a new gummatous area developed on the forehead at the site of an injection, but healed within ten days. A total of eighteen injections were given. There was no change in the Wassermann reaction.

Two patients with gummatous ulcerations of the legs and 2 with nodulous, ulcerative syphilids of the trunk were given ten injections of luetin, with no improvement. They were then given mercury and potassium iodide. The lesions healed rapidly.

One patient with a gumma of the entire nose, extending onto the cheeks, as well as a gumma of the hard palate of eight months' duration, was given ten biweekly injections of luetin. After each injection a severe headache with malaise developed, which lasted about thirty-six hours. The patient felt better physically as soon as the reaction had subsided, but there was no improvement in the local condition, and the treatment was discontinued.

The seventh patient was a Negress, aged 18, with periostitis of the right great toe. The Wassermann reaction of the blood was four plus. A roentgenogram of the bone showed a thickening of the periosteum. After the second injection of luetin, the toe became so painful that the treatment was discontinued, and mercuric salicylate and potassium iodide were given.

Müller and Planner,[22] in 1921, noted a focal reaction in patients with syphilitic gummas following the injection of from 0.2 to 0.5 cc. of luotest. The reaction consisted of an increase in existing pain in cases of periostitis, often a stabbing or prickling sensation in the lesions themselves and an increase in the inflammatory reactions of the gummatous foci, followed by definite improvement of the lesions. The majority of the reactions were seen after the intravenous injection of luetin. They did not think, however, that the reaction was nonspecific as the quantity of the material given was very small, and the reaction was also noticed in some cases following intracutaneous injections. Planner reported cases of obstinate, recurring secondary lesions and cases of malignant syphilis that were no longer influenced by therapy

22. Müller, R., and Planner, H.: Med. Klin. **17**:445, 1921; München. med. Wchnschr. **68**:1393 (Oct. 28) 1921.

with arsphenamine and mercury, which healed with injections of luetin alone or when luetin was given and followed by therapy with arsphenamine. He felt that in cases of malignant and recurring, secondary syphilis (when drug therapy had little or no effect) organic luetin was of therapeutic value in many cases.

SUMMARY

The Kolmer luetin test was performed on 627 syphilitic patients of both sexes and of all ages with all stages of the disease, with and without treatment. Two hundred and twenty-seven nonsyphilitic patients were used as controls.

The following positive reactions were obtained: primary and secondary syphilis (110 cases), 24.5 per cent; latent syphilis (240 cases), 38 per cent; cerebrospinal syphilis (97 cases), 38 per cent; syphilitic gummas (40 cases), 77 per cent; cardiovascular syphilis (23 cases), 48 per cent; congenital syphilis (117 cases), 40 per cent, and babies with negative Wassermann reactions and no syphilitic stigmas, but born of syphilitic mothers (26 cases), 7.5 per cent. Twenty-one of the mothers of these babies were tested. Positive luetin reactions were obtained in 5, 2 of whom were the mothers of the babies with positive luetin reactions. In all groups, there was a higher percentage of positive reactions to the luetin test in the patients with positive serum reactions. Of 227 control patients, 3.5 per cent gave positive reactions and 9 others gave pseudoreactions. One luetin reaction became positive on the third day when herpes zoster developed.

Patients who had received intensive treatment had the higher percentage of positive reactions in the secondary and latent groups, while in the groups with aortitis, gummas and cerebrospinal and congenital syphilis the patients who had received little or no treatment gave the highest percentage of positive reactions.

The female patients showed a higher percentage of positive reactions in the groups with secondary, latent and gummatous syphilis, while in the male patients positive reactions predominated in the groups with cerebrospinal syphilis, aortitis and congenital syphilis. The difference was not marked except in the group with aortitis.

Eighty-four nonsyphilitic and 30 syphilitic patients who reacted negatively to the luetin test were given potassium iodide orally and again tested with luetin. Thirty-one per cent gave positive reactions and 33.5 per cent gave pseudoreactions.

Fifty patients with negative reactions to luetin were given sodium bromide orally, and again tested with luetin. Twelve per cent gave positive reactions and 10 per cent gave pseudoreactions. The reactions were milder than when iodides were given.

A group of patients were tested with the following organic luetin preparations: (1) Kolmer organic luetin, (2) Kolmer luetin prepared with a neurotrophic strain of Spirochaeta pallida, (3) Kolmer luetin prepared from a resistant strain of Spirochaeta pallida, (4) luotest and (5) Busson luetin.

It was found that the organic luetin prepared by the Kolmer method gave a higher percentage of positive reactions than did the luotest and Busson luetin, which are extract preparations. The three types of Kolmer luetin prepared from different strains of Spirochaeta pallida reacted in the same manner.

Seven patients with syphilitic gummas were treated with biweekly injections (from 0.3 to 0.5 cc.) of organic luetin with healing of the lesions in 1 case, improvement in general well-being but no change in the lesions in a second case, and no improvement at all in the other 5 cases. There was no influence on the Wassermann reaction of the blood.

CONCLUSIONS

The question whether or not organic luetin produces a specific reaction in syphilitic patients has precipitated a storm of controversy since the introduction of this test. The fact that a positive reaction does occur in 3.5 per cent of nonsyphilitic patients and can be induced by the ingestion of bromides and iodides makes one consider the test unreliable. These findings, in addition to the fact that the luetin test is not as efficient in diagnosis in any stage of syphilis as the Wassermann test of the blood, is strong evidence that it is not practical.

As to prognosis, there has not been sufficient study of organic luetin to warrant any definite conclusions. The fact that there is such a high percentage of negative reactions in cases in which the Wassermann reaction is positive would exclude it as a means of determining when a patient is cured of syphilis.

In the field of therapy, organic luetin may be of practical value in treating persons with malignant and recurring secondary syphilis who do not respond to therapy with drugs. It has no influence on the Wassermann reaction of the blood and a very inconstant effect on gummatous lesions.

ABSTRACT OF DISCUSSION ON PAPERS OF DR. BARKER AND DR. SCHOCH

Dr. John E. Rauschkolb, Cleveland: In 1933, Ambler reported on the value of organic luetin as a diagnostic test for syphilis in a series of 500 cases. It is interesting to note the remarkable similarity of the end-results in these two reports. The differences are within the realm of statistical percentage variations based on a number of cases in the various series, interpretation of reactions and the technic and reagents employed.

As Dr. Barker has stated, the luetin reaction is evidently a phenomenon based on sensitivity or allergy. Given a host who has an acquired syphilitic infection, this sensitivity comes on slowly, but persistently, and tends to remain positive in the later stages of the disease, regardless of therapy.

In tuberculosis the reaction of the tuberculin is much earlier in the diseased stage and practically permanent.

This may account for the apparently slow reversals of the reaction to organic luetin in syphilitic cases of long standing which are under therapy, as opposed to the Wassermann and Kahn reactions, which depend on the formation of antibodies. Thus this test would have no influence on the other two reactions.

Perhaps this may account for the 3.5 per cent of positive reactions obtained by Dr. Barker in his series of nonsyphilitic patients with associated Vincent's or nonpathogenic spirochetes so-prevalent on the mucous membranes of the upper respiratory and genital tracts. However, this does not explain the positive reactions induced by the ingestion of iodides and bromides. Here an explanation may be offered in the possibility that the inflammation provoked by these drugs, especially on the areas previously traumatized, injured or inflamed, as the areas subjected to the tests, may give reactions pseudo in character but severe enough in clinical appearance to be classed as a positive reaction.

Pharmacologically, we know that these drugs are rapidly excreted or deposited through the mucous membranes or into the follicular elements of the skin.

As a problem in this study, it may be of interest to test the nonsyphilitic patients with positive reactions for bromine by the method devised by Wile and Belote and for iodine by one of the numerous methods at hand. Further, it may be of interest to study the results of ingestion or intravenous injection of sodium chloride in this group of cases.

As to the prognosis so far, only in cases in which late acquired syphilis or late congenital syphilis is suspected and in which the reactions to the Wassermann, Kahn and organic luetin tests are negative is this test of any value.

In the field of therapy, I believe that any improvement attained was not specific in character. Goeckerman, in a recent article, showed the interesting complication of a cutaneous gumma developing after malarial treatment in a patient in whom the symptoms of the central nervous system were definitely improved both clinically and serologically.

In the clinic with which I am associated we have stressed the use of combined foreign protein therapy in the form of malaria or vaccine administered intravenously with vigorous antisyphilitic therapy in our cases of malignant or recurrent secondary syphilis, and the results have been remarkable.

At the present I am not willing to condemn this test completely as a diagnostic procedure. Perhaps it may be perfected to a workable end. Surely in its present stage it is not practical.

Dr. Harry M. Robinson, Baltimore: So far, neither the intradermal nor the percutaneous test is sufficiently reliable to be of value in determining whether or not arsphenamine treatment is to be resumed. It is true that in our experience a strongly positive reaction to the patch test in a patient who has recovered from an exfoliating type of arsphenamine dermatitis is invariably a real danger signal for resuming further arsphenamine therapy. I know of a patient in whom the reaction has remained strongly positive for seventeen years. On the other hand, a negative reaction to the patch test is rarely of sufficient value to warrant returning to the administration of the trivalent arsenicals, except with extreme caution.

In a paper to be published I reported the results of patch tests on 163 persons, of whom 71 had had one or more attacks of arsphenamine dermatitis. A strongly positive reaction was noted in 11 patients, and in all of those of this group to whom we cautiously administered small doses of an arsphenamine a mild exanthem was produced, precluding further use of these drugs. In 55 of the patients with arsphenamine dermatitis the reaction of the patch test was negative. The test was usually performed after a lapse of at least three months following the involution of the dermatitis. Treatment was attempted in several of these patients, and in spite of the negative reactions, cautious treatment with the arsphenamines in 9 patients caused a mild to moderate dermatitis.

Dr. Schoch's conclusion that the intradermal tests are not factors in precipitating a dermatitis is quite in agreement with our findings. In 1930, the group of men with whom I am associated reported on a series of 151 patients tested with the intradermal method, of whom 61 were syphilitic patients who were receiving and continued to receive arsphenamine, yet in none of these did an arsphenamine dermatitis appear at any time.

It is our opinion that the percutaneous, as well as the intradermal, tests are unreliable guides for the resumption of arsphenamine treatment, and we still prefer what Moore calls intravenous testing, which, in the hands of the trained syphilologist, is not a dangerous procedure and is invariably a reliable indicator.

DR. MARION B. SULZBERGER, New York: I was much interested in Dr. Barker's finding of the influence of the administration of iodides on the cutaneous reaction. I have recently been paying attention to the influence of the halogens, iodine and bromine, on cutaneous sensitizations in general, particularly in connection with acne vulgaris. The ingestion of these drugs precipitates the formation of cutaneous lesions in acne vulgaris in a surprising manner.

I wondered if this action of the iodide is specific for luetin. Has this been tested, for instance, in patients with negative reactions to trichophytin and tuberculin? After ingestion of iodide or bromide does one see an increase in the incidence of reactions to tuberculin and trichophytin?

As far as Dr. Schoch's paper is concerned, I think that Dr. Chargin and Dr. Crowley and I were probably the first to call attention to the fact that the positive or negative reactions to the arsphenamine patch test performed on patients who are about to receive (but have not yet received) treatment with arsphenamine is no indication as to the probability of a dermatitis developing from the subsequent therapeutic use of arsphenamine.

However, that is an entirely different question from the one as to whether patients who have had an arsphenamine dermatitis can be divided into two groups: those who react positively to the patch test and those who react negatively; and whether the group with positive reactions will be more likely to have a recurrence of a dermatitis, if arsphenamine therapy is continued. I think that Dr. John Stokes and Dr. Pillsbury have brought some evidence which speaks in favor of this. In other words, a strongly positive test speaks strongly against the possibility of continuing arsphenamine therapy without causing a second dermatitis.

The question of sensitization with arsphenamine is extremely variable. Dr. Simon, of Boston, and I have just reported that one can sensitize guinea-pigs with neoarsphenamine in various cities and in various parts of the country with a variability of ease. In New York it is practically impossible, in Boston quite easy and in Ottawa, as Drs. Williamson and Morrell have shown, it is extremely easy to do so. There are many factors influencing the sensitization from the

intradermal administration of arsphenamine which we as yet know nothing about. Frei and Bilberstein found that it was difficult to sensitize syphilitic persons.

Unfortunately, Dr. Schock did not ascertain whether his patients became sensitized or not. He did not test their skins by means of a second intradermal injection. It seems to me that it would have been interesting, perhaps even necessary, to do this. All in all, Dr. Schoch's results speak rather in favor of the contention that the intravenous administration of arsphenamine tends to counteract the cutaneous sensitization. This is what we have found to hold true in guinea-pigs.

Dr. J. V. Ambler, Denver: In his larger series of cases Dr. Barker reached approximately the same conclusions that were reached by my co-workers and me in our cases at Lakeside Hospital, namely, that the test is a diagnostic aid but is not a practical test. In our smaller series of cases of interstitial keratitis we found 100 per cent positive reactions, and we interpreted this as meaning that in ocular syphilis the test may be of some value. He found 63 per cent, which was also his highest percentage in any group of cases. Therefore, I think the organic luetin test should not be discarded entirely. It still has some value, especially in ocular syphilis.

Dr. George W. Raiziss, Philadelphia: I should like to describe procedures which we employed for the preparation of luetin supplied to Dr. Barker. 1. According to the Kolmer method we made a salt solution extract of a syphilitic testicular tissue, using the Nichols strain for inoculation of the rabbit. 2. The organic luetin from the neurotropic strain was obtained as follows: The rabbit was first inoculated with the Nichols strain of Spirochaeta pallida. Then the testicular syphilitic tissue, finely divided, was injected subcutaneously into mice. These animals acquired syphilis; the brain of the mouse was then removed after bleeding the animal, minced, divided into two portions and injected into the testicles of a normal rabbit. After six weeks, when the primary syphilitic lesion has developed, the testicular tissue was treated with physiologic solution of sodium chloride, and luetin prepared by the Kolmer method. The strain obtained from mice we call the neurotropic strain, since we have the impression that spirochetes, after they pass the body of the mouse, penetrate more easily into the brain, particularly that of a rabbit. 3. Scrapings from a primary lesion of a patient resistant to arsphenamine, also the blood of the same patient, were inoculated into the testicles of normal rabbits. A syphilitic infection was obtained in this way. Testicles of such syphilitic rabbits were used for the preparation of luetin according to the Kolmer method.

Dr. E. B. Tauber, Cincinnati: In regard to Dr. Schoch's paper, we had at the Cincinnati General Hospital a large percentage of arsphenamine dermatitis at our venereal clinic where we give about 200 intravenous injections per clinic day. I was glad to hear what Dr. Sulzberger said about the preliminary test being of little value, because we have drawn about the same conclusions.

We checked with patch tests the cases in which arsphenamine dermatitis developed. Here I am afraid I am going to explode a little dynamite. In our cases, when patch tests were performed with the same type of preparation that had been used for injections, a positive reaction was obtained in a great percentage, but when we used another pharmaceutic preparation we were unable, except in a small percentage of cases, to get a reaction, so possibly we have been giving more attention to the arsenic sensitivity of the preparation than to the preparation itself; possibly the preparation is at fault.

Dr. Maurice J. Strauss, New Haven, Conn.: About a year ago a patient came into the New Haven Hospital with the history that she had contracted syphilis

and that on being treated quite intensively in another city an arsenical dermatitis had developed. This cleared up and she moved to a small town near New Haven. As soon as she moved there (she had had no further treatment) another attack of dermatitis developed, and she came to the hospital with a typical exfoliative dermatitis. She was put to bed and under soothing applications the condition cleared up quite rapidly. On her return home she immediately had another similar attack. This has happened several times, and every time she came into the hospital away from her home environment the infection cleared up. We performed patch tests with arsphenamine, neoarsphenamine and silver arsphenamine all of which gave strongly positive reactions. Not knowing what preparation she was treated with originally we used the ones that we employ as a routine. It is certain that she is not getting any more neoarsphenamine or arsphenamine, and while we have not been able to trace the source, we assume that somewhere in her new environment she is coming in contact with some inorganic arsenic. I should like to ask Dr. Schoch whether any of his patients have become sensitive to inorganic arsenic following a dermatitis from arsphenamine or neoarsphenamine.

Dr. Louis A. Brunsting, Rochester, Minn.: The question of sensitivity to arsenic has interested me for some time. I have tested a group of patients such as Dr. Schoch has described, as well as others, with contact dermatitis, in order to determine a range of sensitivity to arsenic, and I have found that potassium arsenite in a solution of 0.5 per cent is a suitable standard test for sensitivity to arsenic and that there is no correlation between the sensitivity of the skin and the finding of arsenic in the urine and the hair and the nails in abnormal amounts, but that certain of these patients after arsphenamine dermatitis react strongly positively to this standard test.

There seems to be an unusually large number of normal people who react to potassium iodide and potassium bromide by the application of a patch test of an ointment of from 25 to 50 per cent—not only a group such as Perutz has worked with in dermatitis herpetiformis, but a large number of others.

I mention one instance of a man who had syphilis and who was intolerant to drugs except to bismuth. He had a history of arsphenamine exfoliative dermatitis following therapy with neoarsphenamine; he had reactions to mercury in the form of stomatitis and diarrhea, but no dermatitis, and when iodides were given he had a marked enlargement of the cervical lymph glands; he had a marked positive bullous reaction to postassium arsenité, 0.5 per cent, a marked reaction to ammoniated mercury, 1 per cent, and a strongly positive reaction to potassium iodide ointment, 25 per cent. He was able to tolerate bismuth without any evidence of intolerance.

Dr. Leslie P. Barker, New York: In answer to Dr. Sulzberger's question, I have not tested patients receiving iodides with tuberculin and trichophytin. The suggestion that the saline solution used in preparing organic luetin may contain a sufficient quantity of iodine to produce a cutaneous reaction is worthy of investigation.

The objection to Noguchi's culture luetin was the many positive reactions obtained in nonsyphilitic patients receiving iodides. Apparently the same objection can be made to organic luetin.

At some future time an organic luetin may be produced which does not give nonspecific reactions, but at the present time I do not believe it is of practical diagnostic value.

DR. ARTHUR G. SCHOCH, Dallas, Texas: The question of sensitivity to arsphenamine might resolve itself into a geographic problem. In other localities infiltrations may be major factors in producing sensitization. They are no longer regarded as a sign of impending disaster.

In regard to Dr. Brunsting's patient, I have had no experience doing patch tests with potassium arsenite. Four or five years ago I did patch tests with solution of potassium arsenite (pentavalent) in patients who gave positive reactions to the arsphenamine group. They showed no reaction.

In answer to Dr. Strauss' question, this sensitivity has been regarded as a group sensitivity, the arsenobenzol radical probably being the allergen—one may call it that—and a group which is common to all of the arsphenamines, whether old arsphenamine or bismarsen. At Philadelphia patch tests were performed as a routine procedure with both neoarsphenamine and bismarsen, and they invariably checked; when the reaction of one was positive that of the other was positive, and when the reaction of one was negative both were negative.

I accept Dr. Sulzberger's statement that these patients were all syphilitic and, consequently, perhaps more difficult to sensitize. These experiments were an attempt to reduplicate what every one experiences in the treatment room; in other words, faulty technic, a missed vein, usually occurs in a syphilitic patient, and arsphenamine dermatitis usually develops in syphilitic patients, so I felt that the actual circumstances that are taking placec at all times were reproduced experimentally fairly well.

In response to Dr. Robinson, I do not regard the patch test as a "whether-or-not" procedure; it is distinctly a "not" procedure; it is a warning sign of impending disaster and can be interpreted only as such. I feel strongly that a positive reaction to a patch test is an absolute contraindication to further arsphenamine therapy. The reverse cannot be said. Numerous patients show untoward reactions to the arsphenamines and have a negative reaction, but numerous patients have syphilis and have a negative Wassermann reaction. Sometimes the Widal reaction is negative when the patient has typhoid fever. It is asking a lot of a test to be infallible in both directions. I think it gives positive information only.

I disagree with Dr. Robinson's remark about the test dose. I want to condemn it as it is usually advocated. The test dose is approximately one tenth of the usual initial dose. In other words, if the usual initial dose of neoarsphenamine is 0.3 Gm., the test dose is 0.03 Gm. Two patients that I tried to desensitize in Philadelphia were given one ten-thousandth of the initial dose of bismarsen, the mildest arsenical available, with reference to treatment reactions. Both of these patients had a recurrence of the arsphenamine dermatitis. If one ten-thousandth of the initial dose will provoke a recurrence, I think that one tenth of the original dose as a test dose is entirely too large.

THE SAFETY OF LUMBAR PUNCTURE FOR AMBULATORY PATIENTS

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During the past few months there arose the question of performing lumbar puncture in the outpatient department of the clinic for cutaneous and syphilitic disorders at the Stanford University Hospital. Heretofore all of the patients who submitted to this procedure had been hospitalized for at least twenty-four hours. It was realized, however, that to insist on this procedure would result in my being forced to forego valuable serologic control of treatment. The procedure in ambulatory patients was therefore established and has now been in use for more than a year, with results to be described later.

Soon after Quincke [1] first introduced the operation of lumbar puncture reports of accidents began to appear. By 1915 Schönbeck [2] was able to collect reports of 71 fatalities following puncture, a great preponderance being among patients with increased intracranial pressure. Excluding patients with tumor of the brain and other obvious causes of increased pressure, there still remain in the literature reports of a sufficient number of fatalities to indicate that the operation possesses a slight but definite danger to life. Wieder [3] reported 2 deaths in about 27,000 punctures at Ann Arbor. Stokes [4] found 2 fatalities in 15,000 punctures; Sonnenschein,[5] Hammer,[6] Breton and Mizon,[7] Whiteside,[8] Boas [9] and Reusch [10] are among others who reported fatal outcomes following puncture. If the fatalities caused by infection, and therefore preventable, are excluded, the hazard of a fatal outcome is certainly so low that one is not justified in omitting so valuable a method of controlling the treatment of syphilis. However, though few patients

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8. Whiteside, G. W.: New York State J. Med. **25**:937 (Oct. 1) 1925.
9. Boas, H.: Dermat. Wchnschr. **93**:1309 (Aug. 15) 1931.
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die as a result of lumbar puncture, many suffer unpleasant and painful consequences.

The ordinary reaction is headache, more or less severe, occurring within from a few hours to two days following puncture and persisting usually for from two to five days but exceptionally for several weeks. The headache may be accompanied by nausea, vomiting, dizziness and pain in the back.

One of the earliest suggestions regarding the cause of this syndrome was advanced by Sicard,[11] who in 1902 postulated that the symptoms were due to continued leakage of cerebrospinal fluid into the epidural space through the defect in the dura left by the puncture needle. Physical considerations adduced by Reichmann [12] have been held to support this theory. Ingvar [13] showed that methylene blue injected into the cerebral ventricles of cadavers diffuses from the lumbar dural sac following puncture but fails to do so when no puncture has been made. Jakobaeus and Frumerie [14] stated the belief that their success in relieving symptoms by subarachnoid injection of enough physiologic solution of sodium chloride to restore normal pressure supports the theory of leakage. Nelson [15] said that he was able to lessen the incidence and severity of symptoms by plugging the dura with a bit of catgut following puncture. MacRobert [16] agreed that large amounts of fluid may leak out of the puncture wound, and attributed the headache to pressure of the brain on the basilar venous plexus following loss of the cerebral water cushion. Ayala [17] said that symptoms arising within a short time following puncture are due to the disturbance of equilibrium by the removal of the fluid specimen, while trouble arising later is due to leakage.

Opposed to the theory of leakage of cerebrospinal fluid as the cause of postpuncture headaches, Wieder [8] pointed out, is the fact that fluid is known to be rapidly secreted in cases presenting abnormal communications between the dural canal and the surface. Weed and his associates [18] demonstrated that equilibrium exists between the arterial, venous and cerebrospinal fluid systems, and that a disturbance in one is compensated by changes in the others. Wieder suggested that

11. Sicard, J. A.: Le liquide céphalo-rachidien, avec préface du Dr. Brissaud, Paris, Masson & Cie, 1902, quoted by Nelson.[15]

12. Reichmann, V.: Ztschr. f. d. ges. Neurol. u. Psychiat. **11**:581, 1912.

13. Ingvar, S.: Acta med. Scandinav. **58**:67, 1923.

14. Jakobaeus, H. C., and Frumerie, K.: Acta med. Scandinav. **58**:102, 1923.

15. Nelson, M. O.: Postpuncture Headaches: A Clinical and Experimental Study of the Cause and Prevention, Arch. Dermat. & Syph. **21**:615 (April) 1930.

16. MacRobert, R. G.: The Cause of Lumbar Puncture Headache, J. A. M. A. **70**:1350 (May 11) 1918.

17. Ayala, G.: Ztschr. f. d. ges. Neurol. u. Psychiat. **98**:165, 1925.

18. Weed, L.; Wegeforth, P.; Ayer, J., and Felton, L.: The Production of Meningitis by Release of Cerebrospinal Fluid, J. A. M. A. **72**:190 (Jan. 19) 1919.

meningeal hyperemia may be produced in this way, as has indeed been attained experimentally in animals by Ossipow.[19]

Attacking the problem from a different angle, Neustaedter and his co-workers [20] determined variations in calcium content of the cerebrospinal fluids, but found no relationship between the variations and the incidence of postpuncture reactions. Targowla and LaMache [21] divided all of the reactions following lumbar puncture into four types, which they characterize as accidents of: (1) hypotension, (2) hypertension, (3) shock and (4) meningeal reaction. The last-mentioned type is said to be most common.

Regarding the incidence of reactions, all agree that, despite every precaution, symptoms of some degree of severity occur in from 10 to 30 per cent of patients. Stokes, from an experience with about 15,000 cases, fixed the number at from 15 to 25 per cent. Parker [22] reported 20 per cent of reactions in the material from the Mayo Clinic.

Only a few reports are available in the literature regarding the incidence of reactions in ambulatory patients. In a series of 90 punctures, Rahlwes and Loewenstein [23] reported 20 reactions, 15 consisting of mild headache and 5 of more severe headache, with nausea and vomiting. Dattner [24] said that in a series of 1,200 ambulatory punctures he had no unsatisfactory results.

Puncture of ambulatory patients seems to be more prevalent in Germany than in this country. Several authors [25] have described the technic. All of them said that they used some modification of the technic of Wechselmann [26] by which a larger, strong needle is used to penetrate the skin and the supraspinous and intraspinous ligaments, and afterward a very fine needle (0.4 mm. bore) is used to pierce the dura.

METHOD

In the clinic for outpatients punctures are performed in the following way:

Patients report at 1 p. m., after a light lunch. The puncture is performed immediately, with no preoperative medication. Number 18 or 20 gage needles are

19. Ossipow, V. P.: Deutsche Ztschr. f. Nervenheilk. **19**:105, 1901.

20. Neustaedter, M.; Hala, W. W., and Tolstoouchow, A.: Relation of Calcium Content of the Spinal Fluid to Postlumbar Puncture Headache, J. A. M. A. **85**:347 (Aug. 1) 1925.

21. Targowla, R., and LaMache, A.: Presse méd. **36**:1111 (Sept. 1) 1928.

22. Parker, H. L.: Proc. Staff Meet., Mayo Clin. **4**:369 (Dec. 18) 1929.

23. Rahlwes, G., and Loewenstein, J.: Klin. Wchnschr. **5**:1034 (June 4) 1926.

24. Dattner, W.: Wien. med. Wchnschr. **78**:899 (July 7) 1928.

25. Trautman, E.: Deutsche med. Wchnschr. **56**:141 (Jan. 24) 1930. Eicke, H.: Arch. f. Dermat. u. Syph. **155**:136, 1928. Oelze, F. W.: ibid. **155**:135, 1928; Dermat. Ztschr. **53**:457 (April) 1928.

26. Wechselmann, W.: Med. Klin. **20**:1761 (Dec. 14) 1924.

used; the pressure is measured with a plain glass manometer, and from 6 to 8 cc. of fluid is slowly drawn off. The patient is turned on his back; he then rests on the table without a pillow for two hours, after which he returns home, usually on foot or by street car. The operation is performed by medical students, under the supervision of the head of the clinic.

All of the punctures performed in the clinic for syphilitic cases during a period of nine months were tabulated with regard to the occurrence of symptoms, time of onset, duration, severity and response to treatment and were then compared with the last 100 consecutive cases in which the puncture was performed in the hospital. In compiling the list of hospital controls, care was used to exclude all of the cases in which the diagnosis of a disease other than syphilis was in question. Definite cases of tabes dorsalis and dementia paralytica were also rejected. Finally, all of the patients who had received preoperative medication were excluded from the control group; so I feel that the two groups are strictly comparable. Results of the comparison are shown in the table.

Comparison Between Outpatients and Hospital Group Undergoing Spinal Puncture

Data	Outpatient Group		Hospital Group	
	Number	Per Cent	Number	Per Cent
Punctures made	218	....	100	....
Reactions	44	....	22	....
Patients reacting	..	20.1	..	22.0
Reacting first day	26	11.9	18	18.0
Reacting second day	18	8.2	4	4.0
Reacting for one day or less	1	2.3	13	59.0
Reacting for more than one day	43	97.7	9	41.0
Average length of reactions lasting longer than one day	6.7 days		3.1 days	

COMMENT

Several facts of interest are developed by this comparison. First, there is no significant difference in the number of reactions occurring in the two groups. Second, the results in both groups confirm previously reported estimates of the incidence of postpuncture reactions.

Though no greater number of patients escape reactions by hospitalization, this course favors a shorter duration of symptoms. The longest period that any patient in the hospital complained of headache was five days, whereas 1 of the patients punctured in the dispensary complained of intense pain for six weeks. This exceptionally long reaction was excluded in compiling the averages listed in the table. The incidence of reactions in this series—20.1 per cent of all of the patients who had lumbar punctures—checked almost exactly with the figures of Rahlwes and Loewenstein in the only other series of punctures on ambulatory patients that was found.

As a result of this study I feel justified in continuing the practice of making lumbar punctures in the clinic for outpatients. However, for patients able to afford the additional expense, hospitalization is advisable because of the increased comfort and the distinct likelihood of a shorter period of inconvenience.

A study of my data also confirms Nelson's [15] conclusions that no correlation exists between postpuncture symptoms and sex, age or racial groups, or between these symptoms and serologic findings. In short, neither my material nor a study of the evidence in the literature convinces me of the truth of any of the theories advanced to explain the cause of postlumbar puncture headaches or other symptoms. Further investigation of this point is needed.

SUMMARY AND CONCLUSIONS

1. The literature on the cause and the incidence of reactions following lumbar puncture in patients exclusive of those suffering from tumor of the brain or other obvious causes of increased intracranial pressure is reviewed.

2. A comparison between two similar groups of patients, one of which was hospitalized for at least twenty-four hours following puncture and the other of which was permitted to leave the dispensary two hours after the operation, is made with regard to the incidence, nature, severity and duration of symptoms.

3. No significant reduction in the number of reactions following puncture is obtained by keeping patients recumbent in the hospital for twenty-four hours following operation.

4. The average duration of symptoms is, however, materially shortened by keeping the patients in bed for twenty-four hours.

5. The conclusion is reached that lumbar puncture is not too hazardous a procedure for use in the office or the clinic for outpatients, provided every precaution as to asepsis and the exclusion of patients with increased intracranial pressure is used.

6. It is further concluded that the greater comfort of the patient and the chances for a much shorter period of inconvenience justify the physician in advising hospitalization for puncture whenever the patient's financial condition makes such a course not too difficult.

7. It is finally concluded that, despite the wide acceptance of the theory of leakage of cerebrospinal fluid as the cause of the symptoms following lumbar puncture and the advancement of numerous other theories, nothing is known regarding the mechanism responsible for these symptoms.

CLINICAL SPECTROSCOPY

THE QUANTITATIVE RETENTION OF NICKEL IN PSORIASIS; OBSERVATIONS ON FORTY-SIX CASES

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It was a fortuitous anticipation that prompted a biospectrometric [1] analysis in a typical case of psoriasis. The biopsy specimen was obtained from the central portion of a psoriatic lesion the size of a palm on the anterior aspect of the left leg (table 2, case 23). Since the normal metallic constituents of dermal biopsy specimens had been previously determined, the presence of a relatively large quantity of nickel in a psoriatic biopsy specimen was most significant.[2] This report includes the various sources for nickel in human tissue, the incidence of nickel in apparently normal dermal biopsy specimens and the quantity of nickel found in psoriatic biopsy specimens.

While the economic importance of the known deposits of nickel ores in the earth's crust would seem to connote a comparative rarity of this metal, geochemistry has definitely established its universal distribution in soils, plants and animal life. The Danish naturalist Forchammer,[3] in 1854, was the first to report the presence of nickel in arable soils, in the ashes of trees (oak), in sea water and in marine algae. McHargue [4] found appreciable amounts of nickel in various plants in virgin and cultivated soils from three different geologic formations in

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1. Biospectrometric specifies a quantitative spectrographic analysis for the metallic constituents in differentiated and undifferentiated mesoderm, obtained by taking a dermal biopsy specimen with a 3/16 inch (0.47 cm.) punch, the biopsy specimen weighing approximately 0.025 Gm.

2. Gaul, L. E., and Staud, A. H.: Clinical Spectroscopy: A Spectrometric Analysis of Biopsy Specimens Obtained from Cases of Plumbism and Workmen in Daily Contact with Lead Paint, J. Nerv. & Ment. Dis., to be published.

3. Forchammer, J. G.: Ueber den Einfluss des Kochsalzes auf die Bildung der Mineralien, Ann. d. Phys. **95**:60, 1855; On the Composition of Sea Water in the Different Parts of the Ocean, Phil. Tr., London **155**:203, 1865.

4. McHargue, J. S.: The Occurrence of Copper, Manganese, Zinc, Nickel and Cobalt in Soils, Plants and Animals, and Their Possible Function as Vital Factors, J. Agric. Research **30**:193, 1925.

Kentucky. Cornec,[5] using a spectroscopic method of analysis, identified a nickel line as well as lines characteristic of other metals in the ash of seaweeds. The experiments of Verdansky[6] demonstrated the presence of nickel in mosses, plants and various organisms. He cited the tests of Starynkewitch, who found nickel in the ash of the domestic mouse. Bertrand and Mokragnatz,[7] in 1922, reported nickel as averaging 0.015 mg. per kilogram in samples of arable soils, and at a later date determined the normal nickel content of various raw foodstuffs to vary between 0.01 mg. and 2 mg. per kilogram. These observations corroborated Lehmann's[8] studies in 1909, when he found 0.66 mg. of nickel per kilogram of spinach, 0.2 mg. of nickel per kilogram of cow and ox liver and 0.8 mg. of nickel per kilogram of beef. The references which have been cited are sufficient to justify the supposition that the human race in spite of any dietary restrictions or fads is daily ingesting appreciable quantities of nickel or its salts.

Since the discovery of nickel[9] in 1751 by the Swedish metallurgist Cronsted, the chemical and physical properties of this metal were propitious to its extensive application in the sciences, arts and industry. As a corollary to the former statement, it can now be assumed that the utilization of the various metals by man, particularly as it applies to the nickel plating of cooking utensils, water pipes and the various appliances used in the preparation of foods, has greatly increased the normal nickel content of ingested food and water.

The use of nickel as a catalyzer in the hydrogenation or "hardening" of fats is one of the less important sources for its presence in foodstuffs. Offerdahl[10] in a series of 200 determinations for nickel in hydrogenated oils found from 0.5 to 2 mg. of nickel per kilogram of fat. Ellis[11] determined the nickel content of hardened cotton-seed oil to be from 0.02 to 0.075 mg. per kilogram, and oil of palm kernel to be from

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5. Cornec, E.: Etude spectrographique des cendres de plantes marines, Compt. rend. Acad. d. sc. **168**:513, 1919.

6. Verdansky, W. J.: Sur le nickel et le cobalt dans la biosphere, Compt. rend. Acad. d. sc. **175**:382, 1922.

7. Bertrand, G., and Mokragnatz, M. A.: Sur la presence simultanée du nickel et du cobalt dans la terre arable, Bull. Soc. chim. biol. **31**:1330, 1922; Distribution of Nickel and Cobalt in Plants, Ann. Inst. Pasteur **44**:543, 1930.

8. Lehmann, K. B.: Hygienische Studien über Nickel, Arch. f. Hyg. **68**:421, 1908-1909.

9. White, F. B.: Common Commodities and Industry: Nickel, London, Sir Isaac Pitman & Son, 1923.

10. Offerdahl, H. T.: The Catching of Whales and the Technical Extraction and Use of Whale Oil, Ber. d. deutsch. pharm. Gesellsch. **23**:558, 1913.

11. Ellis, C.: The Hydrogenation of Oils, New York, D. Van Nostrand Company, 1914.

0.017 to 0.1 mg. per kilogram. Riess [12] reported similar findings and mentioned that a commercial sample of hardened arachis oil contained 1.8 mg. of nickel per kilogram. Rost [13] also was able to demonstrate minute amounts of nickel in hardened cotton-seed, arachis, linseed and sesame oils. Bordas [14] concluded that the nickel content of hydrogenated oils was approximately 1 mg. per kilogram of fat.

Another extraneous source of ingested nickel followed the adoption of nickel-plated cans, vats and pasteurizing equipment by the dairy industry. While nickel is relatively resistant to the corrosive action of milk, the rapid pitting of containers served to introduce the more resistant alloys of nickel such as Monel metal, nichrome, Alleghany metal and recently stainless steel. Geerkens,[15] in 1883, investigating the corrosion of nickel-plated dairy utensils, found that 2 liters of fresh milk which had been allowed to stand in nickel containers for eight days at room temperature contained 0.022 Gm. of metallic nickel. Donauer [16] recovered 0.56 Gm. of nickel from 500 gallons of sweet milk which had been in contact with nickel during the pasteurizing process. Pratt [17] found that milk pasteurized in a Berndorf-rein nickel receptacle contained 18 mg. of nickel per liter of milk.

Aside from the commercial use of nickel in coinage, its greatest application has been in the manufacture of culinary ware, cutlery, pewter, casseroles and various mechanical appliances to facilitate the preparation of foods. The alloys of nickel, such as German silver (74.3 per cent nickel), nichrome (60 per cent nickel), white bronze (25 per cent nickel), Alleghany metal (8 per cent nickel), Monel metal (65 per cent nickel) and stainless steel (9 per cent nickel), have somewhat replaced the use of nickel-plated and more recently aluminum utensils, since these alloys are more resistant to corrosion and readily take a high and permanent polish. Many investigators have established the

12. Riess, G.: Beitrag zur chemischen Untersuchung gehärteter Fette, unter besonderer Berücksichtigung des Gehalts an Nickel und Arsen, Arb. a. d. Reichsgsndhtsamte. **51**:521, 1919.

13. Rost, E.: Zur gesundheitlichen Beurteilung einiger in der Neuzeit für Genusszwecke empfohlener Fette: I. Tierphysiologische und pharmakologische Untersuchungen gehärteter pflanzlicher Öle (Baumwollsamen-Erdnuss-Lein und Sesamöl) und des ungehärteten Sesamöls, Arb. a. d. Reichsgsndhtsamte. **52**:184, 1920.

14. Bordas, F.: Les graisses hydrogenées dans l'alimentation, Ann. Falsif. **12**:225, 1919.

15. Geerkens, F.: Experimentelle Untersuchungen über die Wirkungen von Nickelsalzen, Inaug. Dissert., Bonn; quoted by Rohde.[20]

16. Donauer, M.: The Action of Metals on Milk, Ice Cream Rev. **5**:78, 1922.

17. Pratt, A. D.: Does the Nickel Dissolved from the Container During Pasteurization Catalyze the Destruction of the Vitamins of Milk? J. Nutrition **3**:141, 1930.

corrosive actions of foods, particularly the sour foods, on nickel-plated utensils and alloys containing nickel.

TABLE 1.*—*The Amount of Metal Absorbed from a 100 Gallon Kettle per Sixty Hour Week When Used in the Manufacture of Acid Foods*

Foods	Nickel, Gm.	Monel Metal, Gm.	White Bronze, Gm.	German Silver, Gm.
Cooking tomato pulp	2.5	0.5	1.7	2.4
Pasteurizing grape juice	1.4	1.7	1.3	0.5
Concentrating apple juice	2.5	1.1	1.4	1.7
Cooking sauerkraut	1.3	0.7	1.8	0.5
Pasteurizing grapefruit juice	5.6	2.1	2.1	1.7

* This table was prepared by Donauer.[18]

Birnbaum,[19] in 1884, in the laboratory of the Polytechnic Institute in Karlsruhe, showed that the quantity of nickel present in food prepared in nickel-plated utensils was directly proportional to the area of plating exposed and the acidity of the food. Riche,[20] a few years later, carried out similar tests and observed that the corrosive action of alkali was negligible, but recovered 115 mg. of nickel from a 10 per cent solution of vinegar and wine containing 11 per cent alcohol and 18 mg. of nickel from beer exposed for ten days to 80 sq. cm. of nickel. Rohde [21] tested the dissolving action of 2 and 4 per cent solutions of acetic, citric, tartaric, lactic and butyric acids on nickel-plating on steel, copper and brass. The loss of weight in the pure nickel pots varied between 2 and 7 mg.; in the plated casseroles, between 5 and 33.5 mg. The quantities of nickel recovered from the test solutions were slightly less than the weights lost by the containers. Ludwig [22] analyzed many samples of food and drink prepared in nickel utensils by means of a gravimetric method of analysis, and calculated the nickel content in milligrams per hundred grams of food. The quantity of nickel present was 12.9 mg. in sauerkraut, 3.5 mg. in plum sauce, 2.7 mg. in spinach, 2.4 mg. in lentils and traces in cooked milk, beef, cabbage, beans and carrots. Dzerzgowsky [23] determined that the quantity of nickel present

18. Donauer, M.: Action of Metals on Fruit and Vegetable Products, Chem. Age **31**:427, 1923.

19. Birnbaum, K.: Ueber die Widerstandskraft von Gefässen aus Nickelplattiertem Eisenbleche gegen organische Säuren, Dingler's Polytechnisches J. **249**:515, 1883.

20. Riche, M. A.: Recherches sur le nickel, J. de pharm. et de chim. **17**:604 1888.

21. Rohde, A.: Ueber die Angreifbarkeit der Nickel-Kochgeschirre durch organische Säuren, Arch. f. Hyg. **9**:331, 1889.

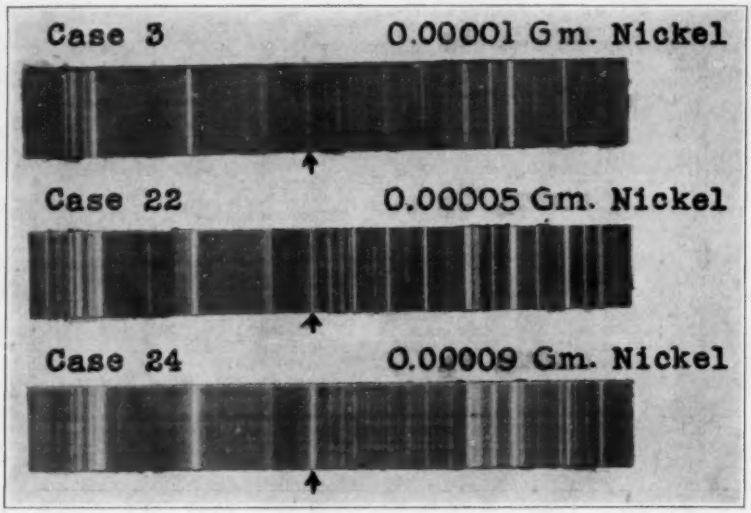
22. Ludwig, E.: Erfahrungen über das Verhalten der Nickelgeschirre im Haushalte, abstr., Chem. Zentralbl. **22**:57, 1898.

23. Dzerzgowsky, W. S.; Dzerzgowsky, S. K., and Schumoff-Sieber, N. O.: Die Wirkung von Nickelsalzen auf den tierischen Organismus, Biochem. Ztschr. **2**:190, 1906.

in foods cooked in nickel utensils varied between 0.02 and 0.32 per cent. Lehmann [8] concluded that the quantity of nickel which can be absorbed by the exclusive use of nickel utensils is about 2 mg. per kilogram in man. Additional references and opinions of various investigators in regard to the effect on health of eating food cooked in nickel utensils are cited in the monograph by Drinker, Fairhall, Ray and Drinker.[24]

BIOSPECTROMETRIC ANALYSES

The incidence of nickel in apparently normal dermal biopsy specimens was established by a study of the spectrograms of 300 biospectrometric analyses. These biopsy spectrograms were representative of



Spectrograms of selected psoriatic biopsy specimens showing variations in the density of the nickel line (3,134.104 angstroms). The quantity of nickel present in the biopsy specimens was calculated from density measurements made with a Moll recording microphotometer.

the various decades and included specimens from premature and full term infants. Spectrograms of the latter group were negative for nickel. The nickel lines were present in approximately 6 per cent of the spectrograms for adults. The quantity of nickel present in apparently normal dermal biopsy specimens was always less than the quantity found in the psoriatic biopsy specimens.

Although a sufficient quantity of nickel was present in a single psoriatic biopsy specimen to give indubitable evidence of a marked retention of nickel in psoriasis, it required additional observation to

24. Drinker, R. K.; Fairhall, L. T.; Ray, G. B., and Drinker, C. K.: The Hygienic Signficance of Nickel, J. Indust. Hyg. **6**:307, 1924.

establish this fact definitely (table 2). All subsequent biospectrometric analyses were made with approximately equal amounts of tissue removed from the central part of psoriatic lesions under identical physical conditions (figure). Being aware of the many sources of contaminations by nickel and its compounds, it was necessary to analyze the instruments and all materials employed in obtaining the biopsy specimens. A spectrographic analysis of the dermal punch, forceps, scissors, needles, alcohol (chemically pure), 70 per cent, acetic acid (chemically pure), 20

TABLE 2.—*Psoriatic Cases Classified According to Age with the Quantity of Nickel Present in the Biopsy Specimen*

Case	Patient	Sex	Age, Years	Duration	Site of Biopsy	Date of Biopsy	Quantity of Nickel, Gm.
1	J. G.	F	8	3 years	Right thigh	1/ 9/34	0.00001
2	H. S.	F	12	2 years	Left knee	1/20/34	0.00001
3	P. B.	M	12	1 year	Right leg	1/18/34	0.00001
4	E. M.*	F	13	6 years	Right leg	1/26/34	0.00001
5	D. B.	M	20	8 years	Sacrum	1/30/34	0.00002
6	L. G.	F	23	20 years	Right leg	1/ 9/34	0.00003
7	I. G.	F	23	6 years	Left leg	1/18/34	0.00002
8	M. K.	M	24	1 week	Back	1/18/34	0.00003
9	B. B.*	F	24	14 years	Left thigh	1/24/34	0.00002
10	J. N.	F	26	5 years	Right thigh	1/20/34	0.00003
11	H. G.†	F	31	3 years	Right sole	3/28/34	0.00004
12	R. S.*	F	31	8 years	Sacrum	3/ 1/34	0.00002
13	S. S.	M	32	7 years	Sacrum	1/30/34	0.00004
14	P. R.*	F	33	9 months	Right leg	12/18/34	0.00001
15	L. Z.	M	35	9 years	Sacrum	2/28/34	0.00002
16	G. H.	F	35	15 years	Left thigh	9/21/33	0.00002
17	W. N.	M	35	3 months	Abdomen	9/19/33	0.00001
18	E. C.‡	M	36	6 years	Left leg	1/12/34	0.00004
19	E. P.	M	36	6 months	Left side of neck	12/23/33	0.00003
20	M. B.	M	40	12 years	Left side of chest	1/ 3/34	0.00003
21	S. K.*	M	40	22 years	Sacrum	1/20/34	0.00003
22	H. L.	M	40	3 days	Left knee	2/20/34	0.00005
23	N. M.	M	40	20 years	Left leg	6/16/33	0.00009
24	S. S.	F	45	2 years	Left knee	12/23/33	0.00009
25	R. G.	M	57	20 years	Abdomen	2/ 8/34	0.00001
26	B. M.§	F	68	15 years	Abdomen	2/16/34	0.00001

* This case was obtained from the Department of Dermatology and Syphilology, Cornell Medical Center, Dr. H. G. Schwartz, Director.
† This was a private patient of Dr. G. M. MacKee.
‡ This was a private patient of Dr. Fred Wise.
§ This was a private patient of Dr. J. Frank Fraser.

per cent, procaine hydrochloride, 2 per cent, and cotton was negative for the presence of nickel.

The following procedure was used as a routine in performing the biopsy:

The psoriatic lesion was cleansed with an alcohol sponge. The central part of the lesion, about the size of a dime, was infiltrated with a 2 per cent solution of procaine hydrochloride. The blanched area was then cleaned with acetic acid, 20 per cent, and dried centrally with a sterile cotton applicator. While preparing the site each patient was questioned concerning the presence of bleeders in the family. After removal of the specimen the wound was painted with compound solution of iodine, and a small pressure bandage was applied. The punch was cleaned after each operation with cotton applicators moistened with acetic acid, 20 per cent solution and alcohol, 70 per cent. Each specimen was placed in a small pyrex test tube which had previously been cleaned with acetic acid, 20 per

cent, and alcohol, 70 per cent, and corked. Nothing else touched the specimen except the platinum forceps used in placing it in the crater of the bottom of the graphite electrode.

For the purpose of determining the quantity of nickel present in the psoriatic biopsy specimens, a series of standard nickel solutions were prepared. These solutions were made by dissolving nickel (99.95 per cent pure) in nitric acid, evaporating the excess acid, and diluting with distilled water until the following concentrations were obtained: solution 1, 1 drop of which contained 0.0000001 Gm. of nickel; solution 2, 1 drop of which contained 0.000001 Gm. of nickel; solution 3, 1 drop of which contained 0.00001 Gm. of nickel; solution 4, 1 drop of which contained 0.0001 Gm. of nickel, and solution 5, 1 drop of which contained 0.001 Gm. of nickel. The nickel line (3134.104 angstroms) was used throughout the tests reported in table 2 for quantitative determinations of that element.

The procedure followed in taking the spectrograms of the standard solution and the biopsy specimens and the method by which the quantity was readily determined have been described in detail in previous publications.[25]

CONCLUSIONS

1. The retention of nickel as a quantitative variable occurred consistently in every case of psoriasis analyzed biospectrometrically.

2. Attention has been called to the natural and extraneous sources of nickel in human tissue.

3. The incidence of nickel in apparently normal dermal biopsy specimens established by a study of the spectrograms of 300 biospectrometric analyses was found to be 6 per cent.

NOTE.—A total of forty-six observations on cases of psoriasis which have been analyzed biospectrometrically has established the presence of nickel as a quantitative variable (table 2). In a series of 300 biospectrometric analyses of apparently normal dermal biopsy specimens the incidence of nickel was 6 per cent and the quantity present was always less than the minimum quantity (0.00001 Gm.) found in psoriasis. Quantitative determinations of other elements present in psoriatic biopsy specimens are now being made in order to determine the rôle of metallic retention in psoriasis.

25. Gaul, L. E., and Staud, A. H.: Clinical Spectroscopy: A Study of Biopsy Material Taken from Patients Receiving Gold Sodium Thiosulphate, Arch. Dermat. & Syph. **28**:790 (Dec.) 1933; Clinical Spectroscopy: II. A Study of Biopsy Material from Patients Who Have Received Intravenous Injections of Silver Arsphenamine, Arch. Dermat. & Syph. **30**:433 (Sept.) 1934.

ACUTE PEMPHIGUS

REPORT OF CASE OCCURRING IN GRANULOCYTOPENIA

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DULUTH, MINN.

In view of the recent interest in granulocytopenia, agranulocytic angina or agranulocytosis—whatever term may be preferred—I report a case of acute pemphigus occurring in a patient with granulocytopenia.

The degenerative changes of the mucous membrane of the throat and mouth frequently seen in granulocytopenia were pronounced in this patient. The sloughing and lesions of the entire large intestine, stomach and esophagus, however, were more like those of acute pemphigus—just as the cutaneous condition was typical of the textbook description of acute pemphigus. The cutaneous lesions occasionally described in granulocytopenia are of a different type from those encountered in this case. The typical granulocytopenic lesions seem to be seated more deeply in the skin, usually with necrotic areas and crusts covering them and with definite enlargement of the regional lymph nodes. However, I have not been able to find any references in the literature to acute pemphigus occurring in patients with granulocytopenia. As a point of interest, in one of Zinninger's [1] cases the patient gave a history of an attack of herpes zoster within half a year preceding her attack of granulocytopenia, and Dr. Landsberg [2] of Berlin described cutaneous lesions in a case of granulocytopenia as similar to those found in herpes zoster. These are the only references I can find which point toward a vesicular or bullous type of cutaneous affliction.

REPORT OF A CASE

A white woman, aged 49, of British descent, whose previous history, dating back in our knowledge to 1923, was irrelevant, on Oct. 30, 1932, suddenly had a severe sore throat, high fever, repeated chills and aches and pains over the entire body. A few days later "blisters" developed in the left submaxillary region. On November 4, the patient was admitted to the hospital, where the white cell count was found to be 900, with no granulocytes present. The temperature on admission was 104.4 F.; the pulse rate, 96, and the respiratory rate, 26. Physical examination gave entirely negative results except for the large bullae, which by this time had spread over most of the face and down on the chest. The bullae developed from

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From the Duluth Clinic.

1. Zinninger, Pauline: Granulocytopenia; Report of Two Cases, J. A. M. A. **102**:518 (Feb. 17) 1934.

2. Landsberg, Manfred: Med. Klin. **26**:1292 (Aug. 29) 1930.

a slight rubbing of the skin, and the outer lining of the bullae consisted of thin epithelium which broke at the slightest manipulation. They contained a seropurulent liquid which later became serosanguineous. The mucous membrane of the throat was sore, reddened and swollen. The treatment in the hospital consisted of six intramuscular injections of 10 cc. of pentnucleotide; an indirect blood transfusion (500 cc.) was made. In spite of the treatment the patient died on the third day after admission. The temperature just before death was 106.8 F., and there were slight coughing and cyanosis. The bullous lesions at this time had involved the entire integumentum except the scalp and scattered small areas here and there on the legs and abdomen.

At no time before the admission to the hospital or during her stay in the hospital had the patient been given barbiturates or amidopyrine.

The pathologic diagnosis after autopsy was: acute pemphigus; emphysema of the lungs, grade II; dilatation of the heart, grade II; fatty change of the liver, grade I; hemorrhages of the mucosa of the esophagus and the stomach; edema of the mucosa of the large intestine; arteriosclerosis of the aorta, grade II, and obesity, grade I. The clinical diagnosis was granulocytopenia and pemphigus. A note from the pathologist said that smears from the bone marrow of the lumbar vertebrae showed numerous myelocytes and less numerous myeloblasts and erythroblasts. No polymorphonuclears were found.

MULTIPLE IDIOPATHIC HEMORRHAGIC SARCOMA OF KAPOSI

REPORT OF A CASE IN AN AMERICAN NEGRO

FRANCIS A. ELLIS, M.D.
BALTIMORE

The racial and national distribution of Kaposi's sarcoma has received much attention in previous articles. In 1932 Dörffel [1] collected 365 cases from the literature and added 16 of his own. The various nationalities or races were represented as follows: Italians, 111; Russians, 50; Jews, 48; Poles, 22; Americans, 13; Austrians, 12; Germans, 8, and Scandinavians, 1. The remaining cases were unclassified because data were lacking. Dörffel's conclusion was that neither race nor nationality plays an important rôle as a predisposing factor. Kren [2] agreed with Dörffel as to the racial variation of this disease; however, neither investigator mentioned the Negro race.

Since Dörffel's report, in 1932, I have found reports of cases in the following races or nationalities: Jews, 5; Italians, 4; Greeks, 2, and Germans, Irish-English and Armenians, 1 each.

In 1931 Pardo-Castello [3] reported a case in a full-blooded Negro, and in February 1932 Andrews [4] presented a case in an American mulatto before the Section of Dermatology and Syphilis, New York Academy of Medicine. These are the only instances that I have found in which the patients were Negroes; the case presented is therefore, I believe, the second on record of Kaposi's sarcoma in a full-blooded Negro.

REPORT OF A CASE

W. J., colored, aged 40, a native of the United States, who had never been outside the country, was first seen in December 1932, in the clinic for cutaneous diseases of the University of Maryland Hospital. He complained of generalized burning and itching. He was apparently a full-blooded Negro, with the physical

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From the Department of Dermatology, University of Maryland.

1. Dörffel, J.: Histogenesis of Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi, Arch. Dermat. & Syph. **26**:608 (Oct.) 1932.

2. Kren, O.: Sarcoma idiopathicum haemorrhagicum (Kaposi), in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 12, p. 891.

3. Pardo-Castello, V.: Sarcoma hemorragico de Kaposi; relación de un caso en un individuo de la raza de color, Bol. Soc. cubana de dermat. **2**:100, 1931.

4. Andrews, G. B.: A Case for Diagnosis, Arch. Dermat. & Syph. **26**:549 (Sept.) 1932.

characteristics of the race, that is, short kinky hair, a large bulbous nose, thick protruding lips and dark skin. He stated that he had received an undetermined amount of antisyphilitic treatment in 1930, and that during the same year a fatty tumor, about the size of an orange, was removed from the left thigh.

The cutaneous condition began two years before the patient entered the clinic with the appearance of lesions on the upper and lower extremities.

Physical examination revealed numerous, pigmented, nonscaly macules up to 1 cm. in diameter on the chest and abdomen. On the arms and legs were many firm, painless cutaneous and subcutaneous nodules, varying in size from about 3 mm. to about 2 cm. The overlying skin was pigmented, and a few of the lesions showed slight scaling. Those over the tibias exhibited a tendency to follow the superficial veins. On the right elbow there was a pedunculated lesion about 1.5 cm. in diameter, which was rather firm. The overlying skin in this instance showed no changes except hyperpigmentation. The ankles were markedly swollen, and the skin over the anterior surfaces revealed a well defined, chronic dermatitis, which extended to the dorsal surfaces of the feet. The eruption was slightly infiltrated and presented a moderately adherent scale, lichenification, fissuring and linear excoriations.

General examination disclosed injection of the conjunctivae and impairment of vision. The blood pressure was 80 systolic and 60 diastolic. The patient had a fissure in the anus and internal hemorrhoids. There was slight anemia, with a normal leukocyte count of 46 per cent lymphocytes. The Wassermann test of the blood was negative.

Two biopsies were made. The first specimen was apparently from a lesion which had recently developed; the second, from an older lesion. The recently developed lesion contained two well defined but nonencapsulated nodules. One was superficial and extended from the subpapillary layer to the middle of the cutis; the other, from the central zone into the fatty layer. The nodules had a slightly infiltrative tendency, but seemed to expand by pushing aside the surrounding tissue. They were composed principally of ectatic, thin-walled blood vessels and spindle-shaped cells with an occasional small lymphocyte. A light mantle of mononucleated cells was also found around the sweat glands and hair follicles. The dilated vessels were lined by a single layer of endothelial cells, and some were supported by one or more pink-staining fibers. Most of the lumens were full of intact red blood corpuscles. The predominating cells were spindle-shaped, with indistinct borders and hyperchromatic and elongated nuclei, which morphologically resembled endothelial cells and which even in areas in which the cells were not closely packed were in direct continuity with the endothelial lining of the blood vessels. Many extravascular red blood cells were found in the infiltrate.

The second biopsy was from a lesion of a more advanced stage. The epidermis showed no noteworthy changes. The infiltrate was less circumscribed than in the former section, spreading in ill-defined strands into the surrounding cutis. The vessels had definitely decreased in number and size, and the nuclei had diminished while cytoplasm was more prominent. The infiltrate was composed of about equal numbers of spindle and round cells, and the large mononuclear elements stressed by many investigators were relatively scarce. Many plasma cells were seen in some areas. The blood vessels were lined with rounder and more cuboidal endothelium than in the first section. There was no more pigment in the nodule than in the rest of the cutis, but it was of a different quality. In the infiltrated areas the elastic tissue had completely disappeared.

Solution of potassium arsenite administered for a period of several months produced a rapid involution of all of the lesions except those over the ankles. The pedunculated nodule on the elbow shrank to a small tag of skin about 2 mm. in length. For the eruption on the ankles, the patient was given 0.5 skin unit of unfiltered roentgen rays semimonthly and a mild keratolytic and antipruritic ointment, which resulted in moderate improvement.

The patient was seen again eighteen months later (May 1934). Edema of the ankles with slight lichenification was still present, but the nodules had completely involuted, leaving residual pigmentation.

News and Comment

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

The meeting of the American Board of Dermatology and Syphilology, scheduled to be held in San Antonio, Texas, from November 13 to 16, has been postponed until the time of the next meeting of the American Medical Association. The oral examination for applicants in Group A and Group B will be held on Monday, June 10, in New York. The written examination for Group B will be held on April 29 in various cities throughout the country.

All applications for this examination should be filed in the office of the secretary before March 10, 1935.

Application blanks and a booklet of information may be obtained from the secretary, Dr. C. Guy Lane, 416 Marlborough Street, Boston.

PROGRAM NOTICE

Applicants for place on the program of the Section on Dermatology and Syphilology of the American Medical Association, which meets in Atlantic City June 10 to 14, 1935, are requested to submit titles and provisional abstracts of their proposed papers to the secretary of this section without delay.

Applicants need not be members of this section but must be Fellows of the Association, graduates in medicine not in private practice or invited guests.

The Canadian Medical Association has been invited to join with the American Medical Association in the scientific program.

HARRY R. FOERSTER, M.D., Secretary,
208 East Wisconsin Avenue,
Milwaukee.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

CALCIFIED EPITHELIOMA OF THE SKIN. K. CH'IN, Am. J. Path. **9**:497, 1933.

Ten cases of calcified epithelioma of the skin examined in the pathologic laboratory of the Peiping Union Medical College are reported. Tumors of this type form a distinct group of neoplasms that are anatomically and clinically well defined. They are circumscribed, well encapsulated growths beneath the skin, consisting of lobulated epithelial masses with a network of usually hyalinized fibrous stroma. The epithelial cells are small, oval, deep-staining and closely packed, and have a marked tendency to undergo necrosis, calcification and ossification. A study of the 10 cases and the 116 instances collected from the literature indicates that the growths are distributed most frequently on the head and neck and occur usually in younger persons. The large majority of the tumors are benign, but a few cases of recurrence following removal have been recorded.

AUTHOR'S SUMMARY. [ARCH. PATH.]

LIPOIDS AND LIPOID DISEASES: II. XANTHOMATOSIS (SCHÜLLER-CHRISTIAN'S TYPE). D. E. LICHTY, Arch. Int. Med. **53**:379 (March) 1934.

In a case of Schüller-Christian's syndrome, in which the patient died and autopsy was performed six months after the onset of symptoms, the osseous lesions were of the type characteristic of the disease.

The only dermal lesions consisted of a papulosquamous eruption on the scalp and in the midline of the chest. These lesions were covered with yellow, oily scales and were confluent on the scalp and fairly discrete on the trunk.

No gross lipemia or cholesteremia was found to suggest a faulty fat metabolism, and the writer does not think that a diet low in fat has any particular therapeutic value.

JAMIESON, Detroit.

NATURE AND ORIGIN OF THE XANTHOMA CELL. L. W. PLEWES, Arch. Path. **17**:177 (Feb.) 1934.

A study of cases of xanthoma and of fatty lesions of the arteries has convinced the author of the identical nature of the xanthoma cell and the foam cell of atheroma, chronic suppurative reactions and certain systemic diseases. Both cells are derived from the reticulo-endothelial system and represent a specific reaction of the cells of the reticulo-endothelial system to certain lipoids when conditions are present which favor their deposition in the tissues.

THE NATURE OF SO-CALLED XANTHOMA. G. GRUENFELD and M. G. SEELIG, Arch. Path. **17**:546 (April) 1934.

The authors review the literature fully to show the chronological development of the conception of the pathology of xanthoma. They subject to a critical analysis the theory that foam cells are always cells of the reticulo-endothelial system which acquire their shape as the result of their phagocytic reaction to the presence of lipoids. On the basis of pathologic anatomy, there are two findings which are not compatible with the theory that multiple xanthoma is a phenomenon of reticulo-endothelial phagocytosis of substances withdrawn from the blood stream: (*a*) the xanthomatosis of the tendons and tendon sheaths and (*b*) the extreme variability of the localization of xanthomatous changes.

A study of the pathologic physiology shows that while hypercholesteremia may be associated with xanthomatous lesions, such foam cell changes may occur with-

out any increase of cholesterol in the blood. In diabetic xanthomatosis, the lowering of the lipocholesteremia by antidiabetic treatment is followed by the involution of the xanthomatous lesions. In other forms of xanthomatosis, however, dietary treatment has no effect on the xanthomas. The etiology of xanthomatosis is still to be determined.

CARO, Chicago.

VIABLE LEISHMANIA DONOVANI IN NASAL AND ORAL SECRETIONS OF PATIENTS WITH KALA-AZAR AND THE BEARING OF THIS FINDING ON THE TRANSMISSION OF THE DISEASE. C. E. FORKNER and LILY S. ZIA, J. Exper. Med. **59**:491 (April) 1934.

Smears were made from the secretions of the tonsils and the nasopharyngeal area of patients with kala-azar. In 60 per cent of the patients examined Leishmania Donovani was demonstrated

Inoculation into animals demonstrated the viability of the organisms from two of the patients.

The writers believe that a great source of the infection in human beings is transference of the organism from person to person by direct contact or through the secretions of the nasal and oral cavities.

OBSERVATIONS ON THE BLOOD CYTOLOGY IN EXPERIMENTAL SYPHILIS: II. THE PERIOD OF DISEASE LATENCY. P. D. ROSAHN, J. Exper. Med. **59**: 721 (June) 1934.

The observations made in this work were based on examinations of the blood made during the period of latency which develops in infected rabbits several months after inoculation. No clinical evidence of syphilis was demonstrable.

Changes were noted in both red cells and hemoglobin, the percentages of both being significantly lower than normal. Other blood cell elements had returned to normal by the time latency had become established.

ON THE PROBABLE INCLUSION OF SEVERAL DISEASES IN THE TITLE '"MOSSY" FOOT.' L. J. A. LOEWENTHAL, Ann. Trop. Med. **28**:47 (March 29) 1934.

Three conditions are discussed and compared: Central American mossy foot, dermatitis verrucosa, and verrucosis associated with chronic edema, for which is suggested the term "lymphostatic verrucosis."

The confusion has arisen from claiming that Central American mossy foot was due to Phialophora verrucosa Thaxter 1915.

As no fungus has been found in the African cases, Rojas has suggested that the cause was lymph pressure.

JAMIESON, Detroit.

KAPOSI'S VARICELLIFORM ERUPTION. W. H. BROWN, Brit. J. Dermat. **46**:1 (Jan.) 1934.

Brown quotes an abstract from Kaposi's book describing a rare type of eruption which occurs as a complication in infantile eczema and reports a case in an infant aged 9 months. He states that only a few cases have been recorded after Kaposi's report of ten cases and that he has found no report in the British or American literature.

The salient features in the reported cases are as follows: 1. The condition occurs in infants with eczema. 2. The onset is sudden, with elevation of temperature and pulse rate for at least twenty-four hours before the eruption appears. 3. The eruption develops with great rapidity; a large crop of lesions may appear over night, and they are most profuse on the face and head. 4. There is high fever for one or two weeks, the temperature ranging from 102 to 104 F., with a fall by lysis. The pulse shows a corresponding rise in rate, to from 130 to 150. There was no marked prostration in the case recorded. 5. The clinical features

of the eruption are described as varicelliform, vacciniform or varioliform. 6. Complete resolution takes place in the majority of cases, though Kaposi and Juliusberg have each recorded a death. 7. Kaposi and others have mentioned the presence of diffuse edema of the skin, in addition to the eruption, and this was present in the case reported. 9. Some degree of pitting, as noted in variola, seems to be a feature. Two excellent clinical photographs accompany the article.

KAPOSI'S VARICELLIFORM ERUPTION. A. D. MCLACHLAN, Brit. J. Dermat. **46**:8 (Jan.) 1934.

A woman, aged 25 years, had had eczema since childhood. A varioliform eruption, associated with diffuse edema, developed on the face, with subsequent involvement on the neck, elbows and wrists. McLachlan states that the condition has not been previously recorded in an adult, and for this reason his case is unusual. He feels that the diagnosis is strongly supported by the occurrence of a preexisting eczematous state and the sudden onset and rapid course of the varioliform eruption, accompanied by acute edema and subsequent scarring in the affected sites. He feels that from the clinical appearances the term "varioliform" seems to be more applicable to this uncommon disease than Kaposi's term "varicelliform." Two photographs accompany the article.

WIEN, Chicago.

CONTRIBUTION TO THE HISTORY, ORIGIN AND DISTRIBUTION OF LYMPHOGRANULOMATOSIS VENEREA IN SOUTH AMERICA. W. E. COUTTS, J. Trop. Med. **37**:97 (April 2) 1934.

Coutts interestingly traces all reports of lymphogranulomatosis venerea, which was known to the Greeks and Romans as "pannus" or "inguen" and to the Arabs as "al-thaun."

Incan pottery depicts lesions very similar to the "genito-anorectal" syndrome.

According to some writers this was a common disease among Negro women in Africa long before the discovery of America.

On the basis of these ancient writings, the author feels justified in assuming that lymphogranulomatosis venerea existed in the countries surrounding the Caribbean Sea before the coming of the Spaniards and that the disease had been introduced there earlier by white persons and Negroes.

Since 1904 an increasing number of cases have been recorded as occurring in Argentina, Chile, Brazil, Venezuela and Bolivia (in the low country). Only two cases have been reported from Colombia.

Two types have been observed: (1) a type with a visible site of inoculation, involvement of inguinocrural lymph nodes and establishment of discharging fistulas; (2) a type with no visble site of inoculation in which fever, headache, etc., develop, followed by involvement of the inguinal and deep iliac lymph nodes, which persist in this state for months but seldom open exteriorly.

Antigens prepared from gland material of both types were specific for each individually.

White women seldom present ganglionar syndromes.

JAMIESON, Detroit.

EXPERIMENTAL CUTANEOUS INDURATIONS IN THE NEW-BORN. HORIA SLOBOZIANO, MARIUS GEORGESCO and P. HERSCOVICI, Bull. Soc. de pédiat. de Paris **30**:165 (March 15) 1932.

One hundred and four infants born at term were studied in the first forty-eight hours of life. In fifty-five the skin was traumatized by pinching or stroking. In 39 per cent of the cases it showed slight induration, and in 3.6 per cent it showed hard plaques. Of a series of twenty-four infants who were subjected to freezing of the skin by means of a spray of ethyl chloride, 70.8 per cent had local reactions; of a series of twenty-five infants who were subjected to freezing and

trauma of the skin, 72 per cent presented similar reactions. Two biopsies, one on skin which had been frozen and another on skin which had been both frozen and traumatized, showed atrophy of the subcutaneous adipose tissue cells, with thickening of the areolar connective tissue cell structure. This histologic picture is similar to that found in the cutaneous indurations of the new-born. Whereas in some instances trauma to the skin may have occurred during birth, in others there was no evidence of this. It is thought that in some cases postnatal chilling of the skin may be a factor in the production of areas of induration of the skin.

Two Cases of Acrodynia; Treatment with Acetylcholine. Henri Janet, Pierre Vallery-Radot and S. Huguet, Bull. Soc. de pédiat. de Paris **30**:644 (Dec. 20) 1932.

Two severe cases of acrodynia occurring in a boy and a girl, each 3 years old, are reported. After they had shown very little, if any, improvement for about a month despite ultraviolet irradiation, they were given six injections of acetylcholine in doses of from 2 to 5 cg. at intervals of two days. The children rested better and showed some abatement of the symptoms after this treatment, but the redness and puffiness of the hands and feet did not change. Both of the patients began to show evidence of the disease in August; in a number of other cases the onset was during the winter and spring months, and it is therefore concluded that the disease is not a seasonal one, as has sometimes been asserted.

Benjamin, Montreal, Canada. [Am. J. Dis. Child.]

Hard Chancre of the Bulbar Conjunctiva. J. M. Renedo and F. R. Gonzalvez, Rev. cubana de oto-neuro-oftal. **6**:286 (Nov.-Dec.) 1933.

A woman of 55 years attempted to remove what felt like a foreign body in the right eye by repeated brushings of the conjunctiva with the corner of a handkerchief. Twenty-five days later she presented a large reddish tumefaction of the mucous membrance of the lower half of the globe; the swelling was indurated, not painful, and oval with flattened borders; its central surface was raised and covered by a grayish-white plaque resembling a pseudomembrane. The lids were swollen; the patient was unable to close them. There was a slight upward displacement of the eyeball; the muscle movements were full except for some limitation of downward rotation. The preauricular gland was not palpable; the submaxillary gland was enlarged. Dark-field examination of scrapings from the mass showed many spirochetes. The Wassermann test was negative.

The case is reported because of the extreme rarity of chancre in this part of the eye. When the eye is involved it is usually the lid that is affected. In those cases in which the mucous membrane is affected, the sites of involvement, in the order of frequency, are the internal angle (especially the semilunar fold), the conjunctiva of the lower lid and lower culdesac, the external angle and the conjunctiva of the upper lid, and the conjunctiva of the globe.

S. L. Rhode, Reading, Pa. [Arch. Ophth.]

Modification of Vaccination for Smallpox by Therapeutic Means. E. Barla-Szabó, Arch. f. Kinderh. **101**:1 (Dec. 19) 1933.

Roentgen irradiation at the site of a reaction to vaccination on the eighth day after inoculation caused disappearance of systemic symptoms such as fever, malaise and loss of weight, and also produced rapid drying of the pustule and decrease in the size of the inflammatory areola. There was no effect when the radiation was applied before the pustular stage. It is claimed that this method does not lessen the general immunity to smallpox. Irradiation is recommended for patients showing an abnormally severe reaction to vaccination, for delicate children and for healthy children in whom an intercurrent disease appears at the height of the reaction.

LeMaster, Evanston, Ill. [Am. J. Dis. Child.]

SYMMETRICAL SQUAMOUS CELL CARCINOMA IN SCARS OF BURNS ON THE LEGS. GEORG ARNDT, Beitr. z. klin. Chir. **157**:305, 1933.

Symmetrical bilateral carcinoma of the extremities developing in scars from burns is reported for the first time. A 44 year old woman had large carcinomatous ulcers on both legs, extending from the region of the ankle to the middle of the leg. The burns occurred 41 years previously. Ulceration developed in the scars after she was 26 years of age. The ulcers healed during several pregnancies, but finally increased in size. Both legs were amputated, and the patient was without recurrence one year after operation. Histologically the tumors were ripe squamous cell carcinomas. Ninety-nine instances of cancer in scars from burns have been collected from the literature. The occurrence in men has been three times as frequent as in women. The average age was 47 years. Carcinoma may develop shortly after a burn or after intervals as long as sixty-nine years. Like other carcinomas of the skin that developing from the scar of a burn is the least malignant form of squamous cell carcinoma and offers a fair prognosis (cures in 62 per cent of the cases).

HELLWIG, Wichita, Kan. [ARCH. PATH.]

DISEASES RESULTING FROM A DISTURBANCE OF FERMENT PRODUCTION (FERMENT DISEASES AND FERMENT THERAPY). JOSEF SELLEI, Dermat. Wchnschr. **97**:1725 (Dec. 9) 1933.

The rôle of the ferment-producing glands, particularly those of the pancreas, stomach and duodenum, has received less attention than it deserves. The author points out that dysfunction of these glands is important in scleroderma, scleredema adultorum, hemochromatosis, hemosiderosis, pernicious anemia and other conditions of the skin and hemopoietic system. The therapeutic use of the ferments is suggested.

LICHEN SPINULOSUS AND FOLLICULAR HYPERSENSITIVITY IN FOLLICULITIS ATROPHICANS SYCOSIFORMIS CAPILLITII. E. ZURHELLE and C. W. BEIJERINCK, Dermat. Wchnschr. **98**:1 (Jan. 6) 1934.

The authors describe a typical case of folliculitis decalvans et atrophicans (Little). They made a vaccine from pus obtained from an abscess that occurred, and injections of this vaccine caused a follicular reaction. This finding, added to the moderate eosinophilia and the hypersensitivity to epinephrine, suggests the possibility that the condition had an allergic basis.

ROENTGEN THERAPY IN LUPUS. E. HESSE, Dermat. Wchnschr. **98**:19 (Jan. 6) 1934.

The roentgen rays should rarely be used in the treatment of lupus vulgaris on account of the danger of damaging surrounding normal skin. The various forms of ultraviolet irradiation and diet are more suitable for the routine treatment of this condition.

CALCIFICATION OF THE GIANT CELLS IN LUPUS VULGARIS. H. O. LOOS, Dermat. Wchnschr. **98**:45 (Jan. 13) 1934.

Histologic examination of a lesion of lupus vulgaris showed calcification of many of the giant cells. In some instances the calcification was complete, while in others it was partial. The calcium was laid down in concentric rings.

CIRCINATE ARRANGEMENT OF EPITHELIAL CYSTS FOLLOWING IMPETIGO CONTAGIOSA. G. NOBL, Dermat. Wchnschr. **98**:50 (Jan. 13) 1934.

Following ordinary impetigo of the face, milia-like bodies appeared in the healing lesions in a circinate arrangement. Various types of therapy, including incision and expression of the individual lesions, failed to cure the condition.

THE ETIOLOGY OF PUSTULOSIS VACCINIFORMIS ACUTA (KAPOSI-JULIUSBERG). HELMUTH FREUND, Dermat. Wchnschr. **98**:52 (Jan. 13) 1934.

A 2¼ year old child had had a dry, scaly skin since birth and eczema for one year. A sudden rise of temperature (to 41 C., 105.8 F.) occurred, as well as general adenopathy and an acute eruption of vacciniform lesions chiefly on the hands and face. New crops of skin lesions appeared on the fourth and eighth days, with a moderate increase in temperature each time. The lesions cleared under applications of soothing ointments in less than three weeks. There was no history of exposure to vaccinia. Material from a fresh lesion was inoculated into the scarified surface of a rabbit's cornea, causing keratoconjunctivitis. Material from this rabbit was similarly inoculated into a second animal, and the eye was removed and sectioned two days later. Many Guarnieri bodies were demonstrated. After the complete recovery of the baby, vaccination was readily accomplished. The finding of the Guarnieri bodies indicates a vaccinia, but the lack of resistance to vaccine contradicts this. The possible explanations for the contradictory facts are discussed.

SKIN LESIONS PRODUCED BY THALLIUM. A. PHILADELPHY, Dermat. Wchnschr. **98**:78 (Jan. 20) 1934.

Three cases of thallium poisoning were observed. In all three loss of hair was complete except on the medial portion of the eyebrows. The lanugo hair was also lost. In one case sharply limited patches of erythema occurred on the fingertips around the nails and on the dorsa of all the proximal interphalangeal joints of the hands. In all three cases transverse bands were observed on the fingernails.

THE DOSAGE OF ROENTGEN RAYS IN DERMATOLOGY IN R UNITS. ERICH UHLMANN, Dermat. Wchnschr. **98**:81 (Jan. 20) 1934.

The author points out the value of the physical measurement of roentgen radiation and outlines his technic for the treatment of various dermatologic conditions. He varies the quality of the radiation (half-value layer) by varying the voltage and by the use of various filters. For most conditions 300 roentgens is given in three equal doses in the course of twenty or twenty-one days. This course should not be given more than three times a year. For epilation in tinea tonsurans 350 roentgens is given to each of the five areas, using a filter of 0.5 mm. of aluminum and a peak voltage of 80 kilovolts (half-value, 1 mm. aluminum).

THE TEETH IN CONGENITAL SYPHILIS. W. SCHWISOW, Dermat. Wchnschr. **98**: 101 (Jan. 27) 1934.

The various opinions regarding the dental stigmas of syphilis are reviewed. The truly pathognomonic conditions involve the central incisors and the first molars. Changes due to anomalies in the development of the enamel, trauma and dental caries must be carefully differentiated.

THE USE OF PARAFFIN IN DERMATOLOGY. LADISLAUS VON CHOLNOKY, Dermat. Wchnschr. **98**:110 (Jan. 27) 1934.

The value of paraffin applied while liquid to various types of skin disease is discussed. The methods of applying it to both circumscribed and extensive lesions are described. It is of particular value on account of the fact that it increases the local temperature for a considerable period. Paraffin apparently increases the activity of sulphur, which may be dusted on the area to be treated before painting or spraying with paraffin.

CHEMOTHERAPEUTIC USEFULNESS OF A GOLD COMPOUND CONTAINING A DERIVATIVE OF A NATURAL SULPHUR ALBUMINOID. W. A. COLLIER and A. WARSTADT, Dermat. Ztschr. **68**:39 (Nov.) 1933.

The gold preparation contains about 9 per cent of metallic gold. The mouse tolerates from 2.5 to 3.3 Gm. per kilogram intravenously and 3.3 Gm. subcutaneously. The chemotherapeutic index for recurrent fever in the mouse was found to be from 1:50 to 1:66 intravenously or from 1:80 to 1:130 by subcutaneous injection. For syphilis in the rabbit the chemotherapeutic index was 1:20 by the intravenous route and 1:60 subcutaneously. In human patients the gold preparation was well tolerated, causing no abnormal symptoms when given in doses of 1 Gm. twice a week.

TAUSSIG, San Francisco.

DIAGNOSIS OF SYPHILIS FROM A DRIED DROP OF BLOOD. ALEJANDRO CHEDIAK, Arch. de med. inf. **1**:3 and 125, 1932. P. DAHR, Deutsche med. Wchnschr. **60**:81, 1934.

The first paper of Chediak was a preliminary report; the second contains the technical details. A drop of capillary blood from the ear or finger is obtained on a glass slide. It is immediately defibrinated by stirring and permitted to dry. The test is best made soon after the blood has dried, but delays of a few days do not interfere with the test. To the dried defibrinated blood is added 0.015 cc. of a solution containing 3.5 per cent sodium chloride and 0.3 per cent sodium carbonate. The mixture is then transferred to another slide within a paraffin ring. The commercial clearing extract for the Meinicke test (M. K. R.) and the already mentioned salt solution are heated separately at 56 C. and then mixed in the proportions of 1:10. Of the mixture, 0.03 cc. is added to the blood. The slide is then shaken for three minutes and kept for thirty minutes in the moist chamber. If the reaction is strongly positive, the reading can be made after ten minutes. When viewed with the microscope, negative tests show brown granules; positive tests, a coarse black precipitate. A comparison was carried out with the Wassermann test (Noguchi antigen), the Kahn test and the clearing test of Meinicke. In a series of 1,005 cases, the Wassermann test was positive in 88 per cent, the Kahn test in 94 per cent, the Meinicke test in 92 per cent and Chediak's test in 86 per cent. The intensity of the precipitate permits a quantitative estimation which compares well with that in the other tests. Chediak's method was checked by Dahr on 600 patients. Of the 475 patients who had given negative reactions to other tests, 467 gave negative reactions to the Chediak test, and 8, or 1.7 per cent, falsely positive reactions. Of the 125 patients who had given positive reactions, 112, or 91 per cent, reacted positively to the Chediak test also.

DAVIDSOHN, New York. [ARCH. PATH.]

DOES THE TREATMENT OF CONGENITAL SYPHILIS PREVENT THE DEVELOPMENT OF INTERSTITIAL KERATITIS? INTERSTITIAL KERATITIS AFTER INJURY. K. VOM HOFE, Klin. Monatsbl. f. Augenh. **90**:492 (April) 1933.

In four cases reported by vom Hofe early treatment of congenital syphilis did not prevent later development of interstitial keratitis. Two of the patients, aged 11 and 13, had received antisyphilitic treatment in infancy; one, aged 12, had had such treatment about nine months prior to observation, and the fourth patient, aged 25, at the age of 14 years, after interstitial keratitis had developed. A recurrence followed in one eye two days after a small foreign body became embedded in the cornea. Numerous deep-seated vessels developed at the site of the foreign body, and parenchymatous cloudiness in its surroundings at a considerable distance. The cornea was fairly clear again a month later.

STOLL, Cincinnati. [ARCH. OPHTH.]

ARGYROSIS OF THE NASAL MUCOSA. ALBANUS, Ztschr. f. Hals-, Nasen- u. Ohrenh. **35**:300 (March 12) 1934.

Albanus describes a case of argyrosis resulting from the ingestion of 9 Gm. of silver nitrate in solution in the course of three years. The skin was deeply impregnated. The mucosa of the nose and ear were less deeply impregnated, but more markedly involved in the regions reached by light than in those in relative darkness. Preparations of the skin and nasal mucosa showed a much greater deposit of silver in the skin than in the mucosa.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

THE USE OF ALCOHOLIC SUSPENSIONS OF SPIROCHAETA PALLIDA FOR THE SEROLOGIC DIAGNOSIS OF SYPHILIS. R. R. HELTZER, Ztschr. f. Immunitätsforsch. u. exper. Therap. **80**:368, 1933.

Spirochaeta pallida was suspended in a solution of alcohol in physiologic solution of sodium chloride. The suspension was used as an antigen for the complement-fixation test for syphilis. It did not become anticomplementary during a period of twelve months, and it became only moderately less sensitive. In a comparative study with other methods the Kahn test proved more sensitive but slightly less specific, while all other antigens were less sensitive than the one prepared from spirochetes.

DAVIDSOHN, New York. [ARCH. PATH.]

BALANITIS XEROTICA OBLITERANS POST OPERATIONEM. JAN OBRTEL, Česká dermat. **14**:121, 1933.

The author reports a case analogous to the one described by Stuhmer in 1928. The patient, aged 36, was circumcised for the relief of phymosis. Soon after the operation (the incision having healed per primam) a urethral discharge appeared, followed two months later by balanitis. Bacteriologic examination demonstrated Streptococcus brevis. No gonococci were found. When the inflammatory symptoms subsided, an atrophic process was evident, and in spite of the treatment the atrophy progressed from the urethral orifice over the glans and the corona glandis. Warm baths and local applications improved the condition considerably. The author advocates greater attention to postoperative asepsis and the application of protective ointments to the glans following circumcision.

SPINKA, Texarkana, Texas.

AUTOVACCINE IN ULCEROUS BLEPHARITIS. K. V. SNEGIREFF, Sovet. vestnik oftal. **4**:208, 1934.

During the past nine years Snegireff has used an autogenous vaccine in 120 patients (210 eyes) suffering from ulcerous blepharitis which had not responded satisfactorily to the routine local and general treatment. The ages of the patients varied from 5 to 45 years and the duration of the disease from one to twenty-five years. In all but 6 patients Staphylococcus aureus was found on bacteriologic examination. The injections, numbering from eight to sixteen, were given subcutaneously into the lid, temple or arm. In 32 per cent a complete cure was obtained, in 55 per cent marked improvement followed, and in 13 per cent there was very little improvement.

SITCHEVSKA, New York. [ARCH. OPHTH.]

A SPECIFIC SKIN REACTION FOR TUBERCULOSIS CUTIS AND TUBERCULID. MASAKAZU KAWABE, Jap. J. Dermat. & Urol. **35**:345 (April) 1934.

Specimens containing the characteristic lesions were excised from the skin of four patients with lupus miliaris faciei and one patient with each of the following diseases: erythema induratum of Bazin, lupus vulgaris, papulonecrotic tuberculid

and phlebitis nodosa tuberculosa. These bits of tissue were then implanted subcutaneously into the abdominal wall of the guinea-pig, and after the pig had died or been slaughtered an aequeous extract of the liver tissues was prepared. This extract was injected in 0.1 cc. quantities, intracutaneously, into the medial aspect of the upper arm in three groups of patients: (1) a group with tuberculous lesions of the skin; (2) a group with tuberculous conditions not involving the skin, and (3) a group without tuberculous disease. In groups 2 and 3 none of the patients reacted to any of the extracts, but in group 1, viz., those with tuberculous lesions of the skin, four of the extracts (from three of the patients with lupus miliaris faciei and the patient with papulonecrotic tuberculid) caused positive reactions in some patients and negative reactions in others. This reaction thus seems to be related to tuberculous involvement of the skin, but the author does not claim that it is shown to be specific by this series of experiments. The reaction shows no relationship with the Pirquet reaction and had become extinct by the end of nine months.

FUNCTION OF ANTIBODY PRODUCTION IN THE RETICULO-ENDOTHELIAL SYSTEM IN THE EXPERIMENTAL SYPHILIS OF RABBITS. M. HANAZONO, Jap. J. Dermat. & Urol. **35**:363 (April) 1934.

Two methods were employed to demonstrate the disturbance in the function of the reticulo-endothelial system in the presence of experimental syphilis in the white rabbit. In the first method, progressive dilutions of the inactivated immune serum of a nonsyphilitic rabbit (rabbit serum immunized against sheep corpuscles) in a simple hemolytic system (washed sheep corpuscles, incubated with guinea-pig serum) were tested at intervals, first in normal healthy rabbits as controls and then in rabbits inoculated intratesticularly with the syphilitic virus. For purposes of study the course of the experimental syphilis thus induced was divided arbitrarily by the author into four periods: (1) the period of latency, (2) the period of development, (3) the period of the acme and (4) the period of healing.

The second method was that of Tokumitu and Imamura, which consisted in the injection of a 20 per cent solution of india ink into a vein of an ear of a white rabbit (approximately 5 cc. per kilogram) and noting the time required for the resultant dark-brownish color of the iris to give way to the normal bright red.

By both these methods, interference with the functioning of the reticulo-endothelial system is postulated, in that the function of hemolysin production and that of removal of the ink from the blood stream set in later and never reach the intensity of those exhibited by the controls in any of the arbitrary periods of experimental syphilis mentioned except the fourth, when of course the rabbit has practically recovered. The inhibition of function is evident in the period of latency and becomes progressively more pronounced during the development and acme of the disease, disappearing gradually with the recovery of the animal from the primary orchitis and epididymitis.

BRENNAN, Chicago.

THERAPEUTIC RESULTS OF USE OF SYPHLOSE IN SYPHILITIC RABBITS. Y. IGA and R. KATAYAMA, Lues: Bull. Soc. japon. de syph. **10**:111 (Dec.) 1933.

Syphlose is an olive oil emulsion of a bismuth compound, the formula of which is $\begin{matrix} C_4\,H_9O\,CO_2 \\ C_4\,H_9O\,CO_2 \end{matrix}\!\!>\!\!\!

Society Transactions

CLEVELAND DERMATOLOGICAL SOCIETY

J. R. Driver, M.D., *Reporter*

Regular Meeting, Jan. 25, 1934

Sidney Littman, M.D., *Presiding*

Tertiary Syphilis, Gummas of the Skin, Hepatitis, Splengmegalia, Hemiplegia and Osteitis of the Right Humerus. Presented by Dr. W. H. Conner.

This white man, aged 55, from the Cleveland City Hospital, had a right hemiplegia at the age of 33, from which he had partially recovered at the end of three months. Since then his general health had been good until six months ago, when an ulcer developed over the upper portion of the sternum following a slight trauma. Two weeks later a swelling developed over the upper outer third of the right humerus which eventually broke down, producing ulceration. During the past year the patient has noticed gradual enlargement of the upper portion of the abdomen.

There is now a crusted, indurated, serpiginous, ulcerative lesion on the sternum in the region of the right clavicular joint. On the outer surface of the upper third of the right arm there is a healing ulceration about 3 cm. in diameter, with roughening and thickening of the underlying bone. On examination, the liver was enlarged, extending approximately 8 cm. below the costal margin. The spleen also showed tremendous enlargement, the lower border extending to the level of the umbilicus. There was marked weakness of the right arm and right leg. The patellar and achilles tendon reflexes on the right side were hyperactive, but those on the left side were apparently normal. The pupils reacted to light and in accommodation. The red cells numbered 3,500,000, and the white cells, 5,100, and the hemoglobin content was 60 per cent. The Wassermann test of the blood was strongly positive. Examination of the spinal fluid gave strongly positive results. The cell count was 1, and there was a markedly increased amount of globulin. The colloidal gold curve read 3443210000. The urine showed a trace of albumin and occasionally hyaline and granular casts.

The patient has received antisyphilitic treatment for the first time during the past six weeks, consisting of disodium-2-hydroxymercurifluoresceine (flumerin), given in doses of 3 mg. per kilogram of body weight for a total of 750 mg., along with potassium iodide. The gummatous lesions of the skin have regressed partially, but there has been no change in the size of the liver or spleen.

DISCUSSION

Dr. John E. Rauschkolb: This is one of the most interesting cases of syphilis that has been seen for a long time. The combination of visceral, osseous, cutaneous and central nervous involvement is most unusual. The marked enlargement of the spleen makes one think of Banti's disease, but this patient possibly has a syphilitic infection of the spleen.

Dr. H. N. Cole: In our excretion studies my associates and I found that flumerin, a mercuric salt, showed a high excretion in the feces. It was thought that perhaps the drug had been excreted by way of the liver, and for this reason we decided to employ it in the treatment of this patient. The case is most unusual; of course one finds few patients who show so many types of lesions due to syphilis. Such patients as a rule respond slowly to treatment.

LATE NODULAR ULCERATIVE SYPHILID OF THE ARM AND HAND, ASSOCIATED WITH ELEPHANTIASIS OF THE LOWER LIP. Presented by DR. E. W. NETHERTON.

This white man, aged 33, contracted syphilis in 1920, and treatment had consisted only of four intramuscular injections until approximately one month ago, when intramuscular injections of bismuth salicylate and the administration of potassium iodide by mouth were instituted. About one year ago he received a blow on the lower lip which produced a slight bruise, which had apparently healed at the end of a few weeks. A month later the lip became swollen to its present size and has remained in this condition. About six months ago a nodular ulcerative lesion about 3 cm. in diameter developed near the left elbow, and a few weeks later, following injury, a similar lesion developed on the back of the left hand, which has not healed.

The ulcer in the region of the left elbow is surrounded by a group of atrophic scars with hyperpigmented margins. The lesion on the hand has partially healed under therapy and shows some atrophic scarring and pigmentation. The Wassermann test of the blood was strongly positive. Permission to examine the spinal fluid has been refused.

DISCUSSION

DR. R. E. BARNEY: I should classify the lesion on the lip as a diffuse syphiloma following trauma.

DR. E. W. NETHERTON: I presented the patient primarily because of the lesion on the lip. This is the second case of this type that has come under my observation, and each followed trauma. In my first case antisyphilitic treatment was ineffective. I believe that the lesion is due to syphilis; it is similar to a lesion described in McLeod's textbook, which occurs also on the male genitalia. The elephantiasis is different from that seen following a streptococcic infection, and it certainly does not resemble lymphangioma.

HEREDOSYPHILIS: INVOLVEMENT OF THE CENTRAL NERVOUS SYSTEM. Presented by DR. W. H. CONNOR.

This white girl, aged 5 years, from the Cleveland City Hospital, is the daughter of a woman known to be syphilitic. She was admitted to the outpatient department of the hospital about six weeks following birth because of a generalized, maculopapular, copper-colored cutaneous eruption, with palmar and plantar lesions, moist lesions about the vulva and anus and bullae on the feet. The Wassermann reaction of the blood at that time was positive, and examination of the spinal fluid also gave positive results. Antisyphilitic therapy was begun, and eleven injections of neoarsphenamine, eight injections of mercury and a course of mercury rubs were given over a period of thirteen months. Attendance at the dispensary was very irregular, and there was a lapse of approximately one and one-half years. At the age of 2½ years the child was admitted to the hospital. At that time she seemed very dull mentally and spoke very little but otherwise showed no clinical evidence of heredosyphilis. The spinal fluid gave a strongly positive Wassermann reaction, contained globulin and gave a paretic type of colloidal gold curve. The child has received therapy steadily since then. There has been marked clinical improvement, but the laboratory findings are still positive.

The patient is now a rather bright child of 5 years, weighing 41 pounds (18.6 Kg.). The skin and mucosae are normal. The pupils react to light. The patellar and achilles tendon reflexes are present, and the gait is normal. There is no definite clinical evidence of heredosyphilis or neurologic findings. The Wassermann test of the blood has been positive on many occasions, and the examination of the spinal fluid has yielded positive findings on all occasions. Treatment has consisted of thirty-nine injections of neoarsphenamine, one course of mercury rubs, twenty-eight injections of mercuric salicylate and sixteen injections of a slightly soluble bismuth preparation. A few injections of typhoid vaccine have also been given. Treatment has been very regular for the last two years.

DISCUSSION

DR. H. N. COLE: The patient was presented to show how resistant syphilis of the central nervous system may be in some heredosyphilitic children and to consider whether it would be advisable to give malaria therapy. If the patient were older I should not hesitate, but the results that my associates and I have obtained with malaria therapy in young children have not been happy. We treated one child 6 or 7 years old, and she nearly died of collapse (convulsions) after a few chills; so we have been rather hesitant about using this treatment in the present case, hoping that the condition would respond to other therapy. We should like to hear the views of the men here.

DR. EUGENE ARDAY: I suggest fever therapy, using diathermy or another substitute for malaria.

DR. H. G. MISKJIAN: In regard to the treatment of congenital syphilis with diathermy, the thermal register is much more fragile in the child than in the adult, and I am afraid that this method would be more dangerous than malaria therapy.

DR. R. E. BARNEY: Might it not be well to try typhoid vaccine in small doses? I think that this treatment would be more easily controlled than malaria therapy and might be of some benefit.

DR. J. R. DRIVER: I suggest further trial of typhoid vaccine, possibly with smaller doses, using the split dose technic.

HYPERTRICHOSIS FOLLOWING IMPETIGO. Presented by DR. W. H. CONNOR.

This Negro child, aged 20 months, from the Cleveland City Hospital, was treated for extensive impetigo in the region of the chin by removal of the crusts and applications of silver nitrate in alcohol, followed by applications of a 5 per cent ammoniated mercury ointment and of potassium permanganate compresses. The eruption was very resistant, and in addition to the aforementioned measures, bismuth tribromphenate ointment and Manson's solution were used before the lesions healed. Following treatment, it was noted that there was a considerable increase in the growth of lanugo-like hairs in the treated area.

DISCUSSION

DR. H. J. PARKHURST: The area shows hyperpigmentation, and this, with the hypertrichosis, makes the lesion resemble a hairy nevus. The appearance of such a lesion following treatment for impetigo is most unusual.

DR. R. E. BARNEY: The fact that the area has been subjected to repeated stimulation by treatment possibly accounts for the hypertrichosis.

DR. CLAUDE B. NORRIS: In my opinion the stimulation produced by the silver nitrate is probably responsible for the pigmentation and hypertrichosis, and the possibility of such a reaction should be kept in mind when this agent is used.

DR. J. R. DRIVER: The effect that one sees as a result of treatment in this case is, to my mind, more apparent than real. The pigmentation will probably be temporary, as will also be the stimulation of growth of lanugo hair, which because of staining by the silver nitrate is more apparent.

RESISTANT SECONDARY SYPHILIS AND PREGNANCY. Presented by DR. E. W. NETHERTON.

This white woman, aged 25, was first seen on Oct. 24, 1933, at which time she presented an early papular secondary syphiloderm with moist lesions on the vulva. She was given an injection of arsphenamine, and the next day she was nauseated. On the third day, after a second injection of arsphenamine, a generalized erythematous eruption developed, which cleared up with injections of sodium thiosulphate. She was given two injections of a bismuth preparation, but the secondary eruption increased rapidly. She was then given silver arsphenamine, receiving 0.45 Gm.

over a period of three weeks. The dermatitis did not recur, nor did it reappear when she was given injections of neoarsphenamine. The syphilitic lesions, however, continued to enlarge and developed into squamous areas, and she was then given injections of a soluble mercury preparation, without effect. About a week ago inunctions of mercury were started, and the lesions on the arms have gradually disappeared, but there has been little improvement in the lesions on the trunk.

She is well developed and well nourished and is about four and one-half months pregnant. Over the shoulders, chest and arms are coin-sized, dull to brownish-red, roughly round and annular, slightly raised, indurated, scaly areas; the scales are large and adherent. The lesions on the arms show evidence of involution, leaving some pigment. These lesions are definitely grouped. There are a few lesions on the legs. There is no ulceration or evidence of previous destruction of tissue.

The Wassermann and Kahn reactions of the blood were 4 plus. Dark-field examination disclosed Spirochaeta pallida. A specimen taken for biopsy from a lesion on the right arm showed a slight amount of hyperkeratosis in the epidermis. There was some edema of the cells of the rete mucosum, and elongation of the interpapillary pegs was noted. The basal cell layer was intact. The interpapillary and subpapillary layers showed edema and dilatation of the vessels, diffuse infiltration by lymphocytes and some hyperplasia of the fixed tissues. Plasma cells were not seen. There was a moderate amount of small cell perivascular infiltration deep in the corium.

DISCUSSION

DR. JOHN E. RAUSCHKOLB: If it is possible, I almost suggest terminating the pregnancy and instituting treatment with malaria. Left as it is, the baby is sure to have congenital syphilis, and there is too great a risk in attempting malaria treatment during pregnancy.

DR. H. N. COLE: Did the eruption appear after the second injection? The description resembled that of a ninth day erythema, and I question whether much stress should be laid on the possibility that the eruption was due to arsphenamine. I should not hesitate to institute further therapy, using neoarsphenamine, through fear that she had an arsenical eruption. Ordinarily pregnancy complicating syphilis does not offer a bad prognosis, as shown by the survey made by a group of cooperating clinics (*Ven. Dis. Inform.* **15**:83 [March] 1934). If sufficient therapy is given the child will be born without evidence of the disease.

DR. E. W. NETHERTON: I appreciate Dr. Cole's remarks in regard to further therapy. My associates and I felt that the eruption was probably not due to arsenic but more likely a toxic manifestation, but we were not sure enough to go ahead vigorously. The patient has had more neoarsphenamine, but intensive treatment was not given because after three injections of 0.6 Gm. of neoarsphenamine the lesions showed no signs of clearing up. However, the treatment was not carried far enough. We thought of giving her a rest and then resuming treatment. The patient's husband had a primary syphilitic lesion which responded to treatment. I recall another case which I presented some time ago in which the husband's lesions cleared up while those of the wife were resistant to treatment.

REQUEST FOR SUGGESTIONS AS TO THERAPY. DR. CLAUDE B. NORRIS.

This man with tertiary syphilis, 44 years of age, came to me with a gumma on the forearm, which I thought was typical because of the strongly positive Wassermann and Kahn reactions. I placed him under therapy with injections of neoarsphenamine, and he got along splendidly; the skin lesion cleared entirely. After giving him twelve injections of neoarsphenamine, along with potassium iodide by mouth, I gave him twenty injections of thiobismol and then immediately resumed the administration of neoarsphenamine, giving him two injections within one week. Following the second injection, he had fever and headache which kept him awake all night. The next day his gums began to bleed. The following

morning he went to a dentist because he could not stop the bleeding of the gums. The dentist noticed some black spots on the mucous membranes of his cheeks, and he had hemorrhagic spots all over the body. His family finally called me, and I gave him sodium thiosulphate intravenously because of the danger of aplastic anemia from arsenical therapy. During the last course of treatment with bismuth there appeared what I took to be an eruption of the type sometimes seen following bismuth therapy, so I have not felt free to return to bismuth therapy. The blood count revealed 3,600,000 red cells and 6,400 white cells, which does not suggest aplastic anemia. What am I to do for the man? Examination of the spinal fluid gave entirely negative results. He is feeling well and does not want any more injections into the arm, and I do not want to give him any.

DISCUSSION

DR. H. G. MISKJIAN: In a case of syphilis of long standing, why push further therapy? The patient seems to me to have toxic purpura following the administration of arsphenamine, although such a reaction is more frequently seen following the use of sulpharsphenamine. I suggest that treatment be stopped until he has recovered from the purpuric eruption.

DR. H. N. COLE: I agree with Dr. Miskjian. In a case of old syphilis with involvement of the central nervous system, what is the necessity of further hurried therapy? Perhaps later he could be given mercury. Was a differential count made on the blood?

DR. CLAUDE B. NORRIS: Yes, and it was normal.

J. R. DRIVER, M.D., *Reporter*

Regular Meetings Feb. 22 and March 22, 1934

M. J. GIBANS, M.D., *Presiding*

TERTIARY SYPHILIS; ANEURYSM OF THE RIGHT INNOMINATE ARTERY. Presented by DR. W. H. CONNOR.

This white man, aged 38, from the Cleveland City Hospital, had been in apparently excellent health until two months ago, at which time he noted numbness and a dull, aching pain in the area corresponding to the distribution of the right ulnar nerve. The symptoms gradually became more aggravated and were accompanied by difficulty in swallowing and an aching pain in the region of the back. He had lost 36 pounds (16.3 Kg.) in weight. There was a history of chancre in 1914, followed by a generalized eruption for which he had received a total of twenty-one injections into the hip over a period of three years.

The man is emaciated and complains of a great deal of pain in the region of the upper part of the back. On examination he showed hypesthesia and dysesthesia of the right arm, corresponding to the distribution of the ulnar nerve. The skin overlying this area was slightly suffused and the superficial veins were prominent. The right upper lid drooped, and the right pupil was myotic and fixed to light and in accommodation. The left pupil was large and reacted to light and in accommodation. The patellar, achilles and arm reflexes were present and equal. The trachea was appreciably deviated to the left, and there was definite fulness in the right supraclavicular fossa. The area of aortic dulness was considerably widened. Tracheal tug and suprasternal pulsation could not be demonstrated. The heart was of normal size, and precordial auscultation revealed no adventitious sounds. Examination of the abdomen and skin revealed nothing abnormal. The patient had a brassy, nonproductive cough. The Wassermann test of the blood has been negative on two occasions.

NOTE.—Following the presentation in February, the patient died, on March 16. Postmortem examination revealed a tumor in the upper part of the right pleural cavity and the adjacent tissues of the neck, with erosion of the corresponding vertebral bodies, producing pressure on the spinal cord. Metastatic growth was present in the right kidney and the axillary lymph nodes. The pathologic diagnosis was: a tumor of the superior pulmonary sulcus (sympatheticoblastoma) of the type described by Pancoast (*J. A. M. A.* **99**:1391 [Oct. 22] 1932).

DISCUSSION

DR. H. N. COLE: Although the serologic reactions have been negative and there are no other physical findings to substantiate a diagnosis of syphilis, the history of a syphilitic infection and of treatment, along with the physical findings mentioned, makes the diagnosis of aneurysm of the right innominate artery the most tenable one.

LYMPHOGRANULOMA INGUINALE. Presented by DR. W. H. CONNOR.

This white woman, aged 26, from the Cleveland City Hospital, acquired a small ulcer on the labium majus pudendi about Jan. 1, 1934, followed by marked swelling in the right groin, for which she was admitted to the hospital on January 15. There is a large swelling in the right groin, with draining sinuses. There is also marked adenitis of the left inguinal nodes, with some involvement of the iliac nodes on both sides. Examination of the rectum revealed nothing abnormal. The Wassermann test of the blood was negative. The Frei test was strongly positive on several occasions. Treatment has consisted of rest in bed, local application of heat and compresses and administration of sedatives.

DISCUSSION

DR. H. N. COLE: The case is interesting because of the involvement of the inguinal nodes in a woman. In women the involvement usually takes place in the nodes surrounding the rectum, no doubt because the primary lesion is usually in the vagina or on the cervix. In this case, however, the primary lesion was on the labium majus.

PSEUDOCOLLOID MILIUM. Presented by DR. JOHN A. GAMMEL and DR. GEORGE W. BINKLEY.

This white man, aged 49, from the Lakeside Hospital, noticed a small papular lesion on the right side of his nose about one year ago. The lesion bled easily and was often treated with a styptic pencil. About six months ago the area began to ulcerate, and a small papule about the size of a split pea developed at the lower margin.

There is now an irregularly shaped ulcer about 5 cm. in diameter, at the lower border of which is a pea-sized granulomatous lesion; there are some small telangiectases surrounding the ulcer. A specimen taken for biopsy from the small nodule showed it to be lined on one side by keratinized epithelium. In the stroma were many cross-sections of hair follicles and sebaceous glands. At one point the epidermis dipped deep into the stroma, so that a cross-section revealed it in the center of the section. Between the epidermis and the level of the sebaceous glands were masses of amorphous, pale-staining, slightly basophilic material which were separated by bands of connective tissue. Special stains showed that this homogeneous material was not mucin or hyalin but was derived from the collagen fibers.

DISCUSSION

DR. H. N. COLE: I agree with the diagnosis of pseudocolloid milium on the basis of the histologic examination, but I should certainly not have made that diagnosis clinically.

PERIADENITIS MUCOSA NECROTICA RECURRENS. Presented by DR. JOHN A. GAMMEL.

This white woman, aged 24, has had "canker sores" on the mucous membranes of the mouth and tongue for about ten years. The lesions persist for approximately two weeks and usually leave slight evidence of scarring. The patient's general health has been good.

There are numerous carious teeth. On the mucous membrane of the lower lip there is a punched-out, superficial ulcer about 7 mm. in diameter, and a similar lesion is present on the right buccal mucosa. Dark-field examination failed to reveal Spirochaeta pallida or Vincent's organisms. The patient has received numerous injections of neoarsphenamine and various local applications without benefit. She was also placed on a low protein, salt-free, high vitamin diet without relief.

DISCUSSION

DR. E. W. NETHERTON: I had the opportunity of studying the patient before Dr. Gammel saw her. I did not think at that time that she had periadenitis mucosa necrotica recurrens, because the lesions did not then show the characteristic punched-out picture and I could make out little or no scarring from previous lesions. From the appearance of the lesions today, I am of the opinion that Dr. Gammel's diagnosis is correct.

DR. R. E. BARNEY: It is hard to differentiate between aphthous stomatitis and periadenitis necrotica recurrens. The distinction between the two conditions, in my opinion, is vague. The lesions of periadenitis necrotica recurrens are supposed to be small nodules at the start, and in the case that Dr. Gammel presents I believe that his diagnosis is probably correct. In my experience in treating several of these patients therapy has been ineffective.

GENERALIZED CARCINOMATOSIS. Presented by DR. W. H. CONNOR.

This white man, aged 27, from the Cleveland City Hospital, states that he had the usual diseases of childhood. There is no history of venereal disease. In November 1933 he became weak, and enlarged, painful nodes began to develop in the left groin. Soon similar adenopathy developed in all the superficial nodes of the neck, axillae, groins, etc. One month ago a generalized papular and nodular eruption developed. One week ago the eyes became swollen, and aphonia developed. The patient has had some fever and has been confined to bed. On examination he appeared emaciated and ill. He spoke in a hoarse whisper. There were reddening and lacrimation of the eyes and pouting of the inner canthi. There was generalized lymphadenopathy, the nodes being discrete, slightly tender and hard. Over the skin there was a widely distributed papular and nodular eruption of a dull reddish color, with little or no inflammatory reaction. The liver and spleen were not palpable. The abdomen was slightly tympanitic. The eyegrounds were normal. Laryngoscopic examination revealed lesions in the pharynx similar to the cutaneous lesions. The prostate was large and boggy. The Wassermann reactions of the blood of both the patient and his wife were negative. The urine contained an occasional white blood cell but otherwise was normal. The blood count revealed: red cells, 3,790,000; white cells, 13,500; hemoglobin, 80 per cent; differential count, normal (2 per cent metamyelocytes).

DISCUSSION

DR. H. N. COLE: Clinically this would be a most difficult case to diagnose. I was asked to see the patient in consultation. He gave a history of illness for several months, fever, loss of weight, generalized enlargement of the lymph nodes and an eruption on the body. On looking at the eruption one immediately thinks of secondary syphilis. The lesions are generally distributed over the trunk. The eruption is shotty, perhaps more so than an ordinary papular syphiloderm, but presents the picture, nevertheless, that one sees in secondary syphilis. There is

generalized involvement of the lymph nodes, more than is generally seen with syphilis. Some of the nodes are very large, hard and discrete. The fever, loss of weight, etc., could also be present in a case of secondary syphilis. When I was told that the Wassermann reaction was negative I was convinced that the condition was malignant syphilis, in which the Wassermann test is often negative. However, there was no primary lesion, and a papule from the skin and a lymph node were removed for examination. These revealed the condition to be generalized carcinomatosis. To produce such a generalized dissemination as this patient has one would expect the primary tumor to be in the lungs, with distribution of metastases by the blood stream.

DR. SIDNEY LITTMAN: This is the third similar case that I have seen; the other two occurred in women following removal of the breast for carcinoma. The involvement spread to other parts of the skin until the entire body was covered with carcinomas and involvement of lymphatic tissues was widespread.

NOTE.—The patient died on April 4, 1934. Autopsy failed to reveal a primary focus. The pathologic diagnosis was reticulum cell sarcoma.

EXTRAGENITAL SYPHILIS IN A CHILD THREE YEARS OLD. Presented by DR. W. H. CONNOR.

H. L., a girl aged 3 years, fell and cut her lip about eight weeks ago. Six weeks later an eruption was noted over the vulva and adjacent areas of the groins and thighs and in the mouth. The lesion on the lip had healed.

There are now numerous characteristic mucous patches over the aforementioned areas. Dark-field examination of a lesion on the vulva revealed Spirochaeta pallida in great numbers. The Wassermann reaction of the blood was strongly positive. Examination of the spinal fluid revealed no evidence of syphilis. The Wassermann reactions of the blood of the father and mother were negative.

LOS ANGELES DERMATOLOGICAL SOCIETY

NELSON PAUL ANDERSON, M.D., *Secretary*

Regular Monthly Meeting, March 13, 1934

STANLEY O. CHAMBERS, M.D., *in the Chair*

A CASE FOR DIAGNOSIS. Presented by DR. NELSON PAUL ANDERSON.

This white man, aged 32, a policeman, has a disease of the skin of six years' duration. This consists of dermatitis and swelling of both hands, forearms and legs and the posterior part of the neck. The past history is essentially unimportant, and all laboratory tests, including determination of the basal metabolism, examination of the urine, a Wassermann test of the blood and chemical examination of the blood, gave negative results. Pollen and plant tests were negative except for questionable reactions to dahlia and apricot. The patient states that the condition has flared up intermittently and subsided again regardless of the numerous therapeutic procedures attempted.

The areas involved include the dorsa and palms of both hands. The hands and forearms are edematous, pit easily on pressure and are twice their normal size. They are bluish and cold. Superimposed on this swelling are vesiculosquamous patches, excoriations and fissuring. The entire skin is thickened. The left foot and leg are swollen, and the condition is similar to that of the hands. Between the toes there is moist, sodden, white epidermis with fissuring. The patches on the left side of the neck have clear centers and are bluish red and scaly. The

border is slightly elevated and vesicular. A biopsy was done, and the tissue cut like cartilage. The histologic changes were psoriasiform.

DISCUSSION

DR. SAMUEL AYRES JR.: I think that this case represents a combination of several conditions. My impression is that of a contact dermatitis with the development of a chronic lymphangitis. I have never seen anything exactly like the eruption, but it is possible that, as it is entirely on exposed areas except for one foot, it may be a contact dermatitis.

DR. MOSES SCHOLTZ: The eruption is acute. It shows a great deal of edema. There are moist, marginated areas which suggest a streptococcic infection. I should call it a pyodermia with a tendency to lymphangitis, almost to the point of elephantiasis.

DR. STANLEY O. CHAMBERS: I cannot help feeling that pathologically this man has a shower of toxins capable of producing an erythema multiforme picture. These repeated attacks, so acute in onset and so symmetrical, with lesions extending up over the sides of the neck and the dorsal surfaces of the forearms and legs, prompt such a consideration.

SCLERODERMA AND (?) CHRONIC ARSENIC POISONING. Presented by DR. SAMUEL AYRES JR.

This white girl, aged 10 years, was first seen on Feb. 23, 1934, because of a generalized hardening of the skin, multiple ulcerations and a generalized exfoliating dermatitis. The onset of the present trouble was about three and a half years ago. She left Los Angeles in April 1930 and took a motor trip to New York, returning early in July. She was entirely well when she left Los Angeles, but when she returned she looked below par, though nothing definite was noted at that time. About three weeks after her return she ceased to be active, i. e., stopped turning cartwheels, etc., because she seemed to be afraid of hurting herself. When she walked her feet seemed to flop heavily. She had difficulty in climbing into bed and could not bend over to pick things up. There were no skin lesions at this time and no systemic symptoms or fever. This state of affairs became more and more noticeable, and a physician was called, who diagnosed the condition as infantile paralysis although the patient had not had any fever. There was an epidemic of infantile paralysis in Los Angeles at that time. The patient was put to bed, and the trunk and legs were put into a shell cast. About one week after being put to bed she suddenly lost the use of her arms because of a flaccid paralysis. About seven weeks later she gradually began to regain movement in the fingers and later in the arms. When she tried to get out of bed she walked on her toes and had no sense of balance. The tendons of the heels were cut, and the feet and legs were put into a cast for six weeks. Following this, the heels touched the ground, and the patient was able to walk awkwardly. About two and a half years ago it was noticed that localized areas of redness and tenderness, apparently rather deep, would develop. These areas would soften, ulcerate and discharge, often remaining open ulcerations for as long as two years. Some are still unhealed. About the same time it was noticed that the skin was becoming hard and that the muscles seemed to be tightening. Dryness and scaling of the skin have been present for over two years, but the skin is less scaly now than formerly. The patient has received much medication, including thyroid for many months, at times in conjunction with pilocarpine, and also ovarian and other endocrine gland extracts. On two occasions she received carbarsone, the last course being in September 1933.

The skin is now diffusely hard and contracted. The patient walks with difficulty, having little motion at any of the joints. The face is involved. The elbows are permanently flexed, and there is atrophy of the palmar muscles. There are several definite keratoses on the palms and soles and many on the trunk,

some of which are about the size of split peas. The skin is diffusely dry, scaly and gray-brown, with an erythematous, blotchy appearance, especially on the face and the backs of the hands. There are five or six partly healed ulcerations varying in size from that of a nickel to that of a dollar with their borders slightly undermined in places and covered with thick yellow crusts. These ulcerations are present on the sides of the left hip, in the left axilla and on the legs. There is a moderately excessive growth of hair over the entire body, including the face.

A twenty-four hour specimen of urine was examined for arsenic by the Gutzeit method and 0.0003 mg. of arsenic per hundred cubic centimeters of urine was found. Sodium thiosulphate was administered by mouth in 5 grain (0.03 Gm.) capsules three times a day, and after five days another twenty-four hour specimen of urine was examined. Arsenic was found in a much larger amount, i. e., 0.001 mg. per hundred cubic centimeters.

In view of these findings it is believed that the scleroderma is secondary to chronic arsenic poisoning, the first manifestation of which was flaccid paralysis of the hands, arms and legs (mistakenly diagnosed as infantile paralysis), subsequent manifestations being generalized exfoliative dermatitis and arsenical keratosis of the palms and soles. The scleroderma is probably an indirect effect of the arsenic poisoning, occurring through some damage to the endocrine or neurocirculatory system.

The findings in this case bear out previously recorded observations on the relationship of chronic arsenic poisoning to scleroderma.

DISCUSSION

DR. C. R. HALLORAN: It seems to me that the condition is primarily scleroderma. The mother stated that the skin showed atrophy before medication. The patient was put to bed and after many months was given some pills containing arsenic. There is a question as to whether or not arsenic when absorbed over a considerable period produces scleroderma. I am not over enthusiastic about this theory. I think that the patient has scleroderma, and whether or not the treatment with arsenic had anything to do with it is problematical.

DR. H. C. L. LINDSAY: When one multiplies the amount of urine passed in a day by 7 to estimate that eliminated in a week and then computes the amount of arsenic passed, the result sounds tremendous. Cases with larger amounts of arsenic than that have been reported by the coroner's laboratory in Los Angeles as being nonpathologic. People taking tonics, containing arsenic, may have considerable arsenic in the urine. Arsenic seems to act peculiarly in certain persons. Some persons who have an idiosyncrasy to arsenic present keratoses, whereas others show nothing but benefit. Many persons show allergic reactions to arsenicals.

DR. SAMUEL AYRES JR.: I want to correct a misconception of Dr. Halloran. I did not feel that the carbarsone given was the cause of the scleroderma, although it may have aggravated it. When the patient came back from the trip she walked peculiarly and was weak. She was put to bed in a cast under the assumption that she had infantile paralysis although she had not been ill, and one morning she awoke and could not move her arms. My thought was that she might have been poisoned by arsenic from fruit or vegetables eaten while traveling, and that the paralysis might be due to arsenical neuritis. Lesions which look like arsenical keratoses have developed on the trunk and palms. The girl showed a trace of arsenic in the urine at the first visit, but after having been given sodium thiosulphate for several days the amount of arsenic was increased nearly ten times. I think that the condition is interesting, but I doubt if therapy can do much good.

GRANULOMA OF UNDETERMINED ETIOLOGY CURED BY MAGGOT THERAPY. Presented by DR. SAMUEL AYRES JR.

Dr. D. G., aged 36 years, was presented at a meeting of this society about a year ago for suggestions as to therapy. He is shown again to illustrate a successful

termination of a steadily progressing granulomatous ulceration by the use of an unusual therapeutic measure.

The lesion began about nineteen months ago, or nine weeks before the patient came under observation by my associates and me. According to the patient, the lesion appeared rather suddenly and consisted of a palm-sized area of redness and induration on the upper anterior aspect of the left thigh. There was fever, the temperature reaching as high as 102 F., for about a week. The area was incised, and about an ounce (30 cc.) of pus was obtained. Prior to the onset of the lesion on the thigh the patient had had epidermophytosis of the feet and several infected mosquito bites on the ankles. About a year before the onset of the lesion on the thigh, the patient had had his left hand amputated in Shanghai, China, as the result of a streptococcic infection following paronychia.

When first seen, on Oct. 11, 1932, the lesion on the upper anterior aspect of the left thigh consisted of a rather deep, granulomatous ulceration the size of a silver quarter. The base was uneven, and the edges were somewhat undermined. The inguinal glands were not noticeably enlarged. The feet were normal except for markedly hypertrophic nails on the great toes and some thickening of several other nails.

In spite of various types of treatment, the lesion continued to spread. Its most rapid extension occurred after attempted excision with the cautery, at which time an attempt was also made to suture the edges. The various types of treatment given may be summarized as follows: cauterization with phenol and iodine; actual cautery; excision by the endotherm knife; administration of iodides intravenously and by mouth; ultraviolet and roentgen irradiation; intravenous injections of autogenous vaccine (containing a diplococcus and a hemolytic streptococcus); two injections of neoarsphenamine; six injections of antimony and potassium tartrate; administration of fuadin; bacteriophage therapy; ten injections of gold sodium thiosulphate, and local application of compound solution of copper and zinc sulphate (Alibour's solution), Castellani's carbol fuchsin paint, tincture of metaphen, maggots (for about two months) and eucalyptus charcoal.

The treatment by maggots overlapped the treatment by gold sodium thiosulphate, but at the conclusion of the injections of the gold compound the ulceration was not much improved except that the maggots had cleaned out a good deal of the necrotic tissue.

The maggot treatment was suggested by Dr. Mosser Taylor, who had used it successfully in chronic osteomyelitis. The details of the treatment will be described in a formal case report. The maggots were changed about every five days. At the conclusion of the maggot treatment, the wound began to heal, and the process was apparently greatly stimulated by the daily application of powdered eucalyptus charcoal.

The results of laboratory procedures were as follows: The Frei test was negative. The Kahn test was negative. Cultures revealed a hemolytic streptococcus, a diplococcus, Staphylococcus albus and Staphylococcus aureus. Two fungi which resembled Epidermophyton interdigitale and Epidermophyton cruris, respectively, were grown on Sabouraud's medium from a toe-nail. A fungus of undetermined identity was grown from the thigh on one occasion only. It died after a few weeks. Numerous other cultures from the lesion on the thigh planted on Sabouraud's medium both aerobically and anaerobically were negative, and no fungi were ever found by direct examination of pus.

A biopsy failed to identify the lesion, and smears from the biopsy specimen and from the ulcer directly were negative for Leishman-Donovan's bodies.

DISCUSSION

DR. SAMUEL AYRES JR.: I cannot remember the formula for fuadin. It is a new antimony preparation supposed to be particularly beneficial in infections of the leishmaniasis group, but the lesion showed absolutely no improvement after six or eight injections, nor did it improve under antimony and potassium tartrate.

Nothing did any good until maggot treatment was instituted. I am not aware of maggots having been used before in dermatologic practice. Whatever the cause of this disease, it seems to have been cured by the maggots. All dermatologists occasionally see chronic ulcerating granulomas of undetermined origin, and maggot therapy might be of value in such cases.

COCCIDIOIDAL GRANULOMA. Presented by DR. H. P. JACOBSON.

This woman was presented before this society about a year ago. At that time she showed an active coccidioidal infection with marked destructive ulcerative lesions involving the upper lip, nose and adjacent parts of the face. The patient has been under treatment since that presentation, and I am presenting her again to show the results following systemic treatment.

DISCUSSION

DR. H. P. JACOBSON: The type of coccidioidal infection which the patient had was the most serious kind, which in my experience has terminated fatally in 100 per cent of the cases. The contrast between the patient's former condition and her appearance today is obvious enough to require no comment. I tested the effect of fuadin on this patient, and the results derived therefrom were anything but favorable. While she was under treatment with this drug the cutaneous lesions flared up markedly, and her general condition suffered correspondingly. Another interesting feature in this case is the fact that, in addition to the coccidioidal infection, the patient has a tuberculous infection. She was operated on for an extensive fistula in ano, and the resected granulation tissue revealed the presence of tubercle bacilli. About a month ago the patient had a hysterectomy performed for multiple uterine fibrosis, and she has been out of the hospital for only ten days. I might mention that for a time the patient was receiving tincture of iodine per os, imbibing as high as 100 drops three times a day, with a good deal of benefit and with no exacerbation of the tuberculous infection. As can be seen, in spite of the double widespread infection (tuberculosis and coccidiosis), the patient has made remarkable progress and, from all evidence at hand, is well on the road to complete recovery.

DR. SAMUEL AYRES JR.: Was the treatment a combination of coccidioides vaccine and colloidal copper?

DR. H. P. JACOBSON: Yes.

DR. STANLEY O. CHAMBERS: Did the woman have active pulmonary tuberculosis?

DR. H. P. JACOBSON: Yes.

NELSON PAUL ANDERSON, M.D., *Secretary*

Regular Monthly Meeting, April 10, 1934

STANLEY O. CHAMBERS, M.D., *in the Chair*

TELANGIECTASIA OF THE FEET. Presented by DR. N. P. ANDERSON.

This white woman, aged 30, has had a cutaneous disturbance on the ankles and feet for one year. She states that she had a small birthmark on the inner aspect of the left foot near the heel. This remained about the same until one year ago, when she began to note increasing redness of the foot, which began at the bottom of the foot and spread upward. At about the same time a similar redness appeared on the right foot and leg. She has never had scarlet fever or any thyroid disturbance, and her basal metabolism was normal in June 1933. She had pneumonia at 11 years of age, intestinal influenza in 1924 and pleurisy in 1928, which confined her to bed for two weeks. She has never been pregnant, and her work as a telephone operator does not require much standing.

The dorsa of the feet and the lower parts and sides of the ankles down to the edge of the area covered by her slippers now present marked redness and purplish redness, which is apparently entirely due to capillary dilatation and telangiectasia, as the color can be entirely expressed by stroking the skin downward. On standing, some varicosities are present about the ankles, but there are more marked varicosities about the posterior aspects of the knees.

DISCUSSION

DR. MOSES SCHOLTZ: All I can see is telangiectasia. I think that one can put this label on the condition and confess ignorance as to its etiology. There is no visible atrophy. Sometimes syphilis is responsible for an eruption of this kind.

DR. W. H. GOECKERMAN: I agree with Dr. Scholtz. The patient should be studied carefully in an endeavor to determine the cause of the condition.

A CASE FOR DIAGNOSIS. Presented by DR. N. P. ANDERSON.

E. S., aged 19 years, has a generalized cutaneous disturbance of five year's duration. Her past history is unimportant. She presents numerous flat papular lesions on the backs of the hands, the dorsa of the feet and the lower part of the neck.

Histologic examination of a section revealed that the epidermis was slightly thickened over a small area, especially the keratin layer, which was four or five times the normal thickness. The papillae were slightly elongated. There were no changes in the cutis and no evidence of malignancy. The diagnosis was: a small localized patch of hyperkeratosis.

DISCUSSION

DR. SAMUEL AYRES JR.: The lesions do not coincide with my idea of a flat wart. I have never seen juvenile warts on the palms and the sides of the neck.

DR. C. R. HALLORAN: Clinically the condition is verruca plana juvenilis. The occurrence of lesions on the palms is unusual.

DR. W. H. GOECKERMAN: Morphologically the lesions resemble verruca plana juvenilis, but the distribution is most extraordinary.

DR. MOSES SCHOLTZ: It is possible that the lesions are flat warts, but not all of them are flat. Many are almost filiform. Some are yellowish and softer than usual. They must be benign tumors, but I think that they will not prove to be verrucae.

DR. N. P. ANDERSON: I am not very familiar with the histologic characteristics of flat warts, for biopsy is rarely performed on such lesions. The epidermal changes in the histologic section in this case are consistent with what I think a flat wart should show. There is a considerable amount of hyperkeratosis, more than one would expect on looking at the lesions clinically. I do not know what the condition is. I have treated the patient for flat warts with bismuth and yellow mercurous iodide, with no effect. Although I made a diagnosis of that condition at first, I am not convinced that the lesions are flat warts.

DARIER-ROUSSY'S SARCOID. Presented by DR. STANLEY CHAMBERS.

This man, aged 22, has a generalized cutaneous disturbance which began in February 1934 at the site of a pin prick. A dull erythema with edema appeared over the thumb and the thenar eminence. There was no pain or tenderness and apparently no systemic complaint. The lesion continued to develop upward over the right forearm to the elbow. It was at all times well marginated. Healing slowly took place, leaving an atrophic, scaly cutis with deposition of considerable pigment. About seven days after the onset, a similar dull red, edematous plaque appeared on the left side of the forehead over the eyebrow. This was followed by numerous similar lesions on the left cheek. The Wassermann reaction of the

blood has been repeatedly negative. There have been no constitutional complaints, fever or local discomfort. The microscopic section was frankly tuberculous. Hansen's bacilli were not found by special staining. The cutaneous lesions have almost faded following the oral administration of a solution of potassium arsenite. An atrophic, pigmented skin remains.

DISCUSSION

DR. MOSES SCHOLTZ: It seems to me that the lesions are of two different types. Those on the face might be sarcoid, but I cannot conceive of the lesion on the arm being sarcoid, as it is too extensive and too superficial. For that reason I should rather consider the possibility of leprosy, which may show both types of lesions.

DR. SAMUEL AYRES JR.: I think that the condition is leprosy. The patient cannot distinguish between the touch of a finger and a sharp pin prick. The ulnar nerve is easily palpable on the affected side.

DR. SAUL ROBINSON: My diagnosis is leprosy. I palpated a large ulnar nerve. Moreover, the loss of sensation is significant.

DR. E. D. LOVEJOY: There are two features in this case which rule out leprosy, namely, the lack of symmetry of the lesions and the palpable enlargement of only one ulnar nerve.

LUPUS ERYTHEMATOSUS. Presented by DR. STANLEY O. CHAMBERS.

This white man has an eruption of several years' duration which began on the elbows and knees. He was treated for psoriasis. New lesions appeared on the neck and the mandibular ridge about one year ago. During the past five months the lesions have increased in number and have appeared on the forearms and hands. An associated adenitis has been present in varying degrees since the appearance of lesions on the face.

DISCUSSION

DR. SAMUEL AYRES JR.: This case is extremely interesting. If one saw only the lesions on the elbows and knees, one would make a diagnosis of psoriasis, but the color is peculiar. The lesions on the face, I think, are typical of lupus erythematosus. One of the most striking features is the extreme adenitis. The glands in the groins are nearly the size of a hen's egg. I suppose that studies of the blood have been made to rule out leukemia. There seems to be some systemic toxic absorption, tuberculous or otherwise.

DR. C. R. HALLORAN: I believe that the cervical adenopathy is distinct from the cutaneous manifestations.

DR. KENDAL FROST: The picture as a whole somehow does not fit my conception of lupus erythematosus. The lesions on the face could well be that disorder. However, those on the elbows are definitely papular and resemble psoriasis, and the lesion on the knee is more like lichen planus. Is it not possible that the patient has different types of lesions? Perhaps the lesion on the knee could even be considered sarcoid.

DR. W. H. GOECKERMAN: I agree with the diagnosis of lupus erythematosus. Dr. Ayres has expressed the thoughts that ran through my mind when I saw the patient. Further studies of the blood should be made to rule out lymphoblastoma. That condition should be kept in mind even though the blood is now normal.

DR. STANLEY CHAMBERS: The section was taken from the lesion on the elbow. The histopathologic picture was frankly tuberculous.

A CASE FOR DIAGNOSIS. Presented by DR. H. C. L. LINDSAY.

Mr. R., has a habit of continually scratching his head, and a partially bald spot has resulted. There is some keratosis around the bases of the hairs, but no inflammation is visible macroscopically and no infiltration is apparent in the slide.

DISCUSSION

DR. MOSES SCHOLTZ: Since the patient is a Negro I refuse to make a definite diagnosis.

DR. C. R. HALLORAN: Grossly this case resembles one of idiopathic trichoclasis that I reported about two years ago. There is no alopecia or apparent pathologic change of the scalp but merely patches in which the hairs are broken about 6 or 8 mm. from the scalp. I believe that if hairs from these patches are studied microscopically it will be found that their distal ends are frayed. Possibly in the edges of the patches will be found hairs in which nodular swellings may be observed. At this point the hair will break. Patients with this malady resist any form of treatment. Little is known as to the etiology of the condition.

DR. H. C. L. LINDSAY: I consider that the condition is merely alopecia artificialis. The man undoubtedly scratches his head from morning to night and has worn the hair off, but I was unable to find any nodules in the hair.

CAVERNOUS LYMPHANGIOMA? Presented by DR. SAUL ROBINSON.

Miss I., 20 years old, has had the present condition on the left hand, involving the third and fourth fingers, since she was 5 years of age. There has been slow growth of the lesion for many years.

DISCUSSION

DR. SAUL ROBINSON: I should like to hear some suggestions regarding therapy in this case.

DR. MOSES SCHOLTZ: A diagnosis of a lymphangioma seems to be indicated; but if the condition is that disease it must be a very unusual form. It may be a diffuse lymphangioma duplicating the anatomic contour of the fingers, and I wonder if one could not consider as an alternative diagnosis myxedematous degeneration of the skin. There is no feeling of vascular loops on palpation. The case is very unusual.

DR. H. S. CAMPBELL: I think that one has to consider more than simple lymphangioma. The lesion has not the typical color of lymphangioma. I should not consider myxedema of the skin because the lesion is too deep. There are three possible diagnoses, to my mind: lymphoma proper, lipoma and synovial fluid degeneration of some type. The suggestion is in order that the condition is surgical rather than dermatologic.

DR. C. R. HALLORAN: I believe that the treatment should be surgical.

A CASE FOR DIAGNOSIS. Presented by DR. H. P. JACOBSON.

This Chinese man, aged 50, the father of several healthy children, the youngest of whom is 7 months old, was first seen about three weeks ago for the treatment of an eruption of three years' duration which had its inception while he was on a visit to China. He has been under the care of several physicians in the past three years, none of whom have afforded him any permanent relief. He complains of a good deal of soreness and itching in the scapular and interscapular regions, which on occasion has kept him awake at night.

He presents a cutaneous eruption involving symmetrically the scapular and interscapular regions in butterfly-shaped fashion. The eruption consists of fairly uniformly sized inflammatory papules, rather closely placed, varying from bright red to a purplish-violaceous hue and associated with some fine scaling. Below the border of the eruption under the right scapula are several sharply marginated circular and oval plaques varying in diameter from 1 to 2 cm., with elevated scaly borders and somewhat depressed centers and of a purplish-violaceous hue. In the region of the right eyebrow and for about 0.5 cm. above the hair margin is a sharply marginated semicircular plaque about 2 cm. in diameter, deep red and rather infiltrated. Another irregularly shaped plaque, slightly elevated and con-

forming in general character to the lesion of the right eyebrow may be observed on the right side of the neck below the mandible. The ulnar nerves are easily palpable in their grooves and seem thickened. The gingiva over the upper incisors is hypertrophied, and the teeth are in poor condition.

Direct smears from the suspected gingiva revealed streptococci, medium-sized chains, diplococci and spirilla but only a few fusiform organisms. Repeated nasal smears have thus far failed to reveal Hansen's organisms. The Wassermann reaction of the blood was negative. Microscopic study of a biopsy specimen failed to reveal anything other than a nonspecific inflammatory reaction involving the whole cutis and to a degree the epidermic layers. No lepra cells or bacilli were observed in the sections.

DISCUSSION

DR. MOSES SCHOLTZ: When one sees an Asiatic patient the first possibility that comes to one's mind is leprosy. The lesions on his face morphologically might be leprosy, but the lesions on the back are rather difficult to accept as leprosy. They are rather hard and dry. To my mind, the condition is follicular keratosis or may be one of the spinokeratotic lesions to which the yellow races are predisposed.

DR. H. C. L. LINDSAY: I could not ascertain that the man has leprosy, but I have seen lepers with similar eruptions.

DR. W. H. GOECKERMAN: I could not find enough evidence to make a diagnosis of leprosy. Though I realize that the cutaneous manifestations of that disease are multiform and bizarre at times, this condition seems to be only a dermatitis, and the peculiarly sharp outline of the lesions suggests that the cause is some external irritant. I cannot say anything more definite without further study.

DR. C. R. HALLORAN: The lesion on the right brow simulates leprosy. Those on the back are quite different; they are apparently grouped vesicles. I believe a consideration of Duhring's disease is warranted.

DR. N. P. ANDERSON: When Dr. Goeckerman and I were getting the history the patient said that the lesions in the scapular regions were of only about four weeks' duration, and further that they disappeared and reappeared. It is possible that the condition is a dermatitis venenata from the back of a chair.

BRONX DERMATOLOGICAL SOCIETY

HENRY SILVER, M.D., *Secretary*

Regular Meeting, March 22, 1934

SAMUEL FELDMAN, M.D., *President*

A CASE FOR DIAGNOSIS. (TUBERCULOSIS?). Presented by DR. MARION B. SULZBERGER for DR. I. STEIN.

This man, aged 22, was admitted to the Montefiore Hospital in October 1931, complaining of abdominal cramps, diarrhea, bloody stools and progressive loss of weight of about six months' duration. A diagnosis of ulcerative colitis was made, and the patient was given exhaustive medical treatment, including six or eight blood transfusions, without avail. An ileostomy was performed in December 1931 after the intestine had perforated and peritonitis had set in. The postoperative course was uneventful. The pains disappeared, and the patient gained in weight and was discharged in February 1932.

In the spring of the same year he fell down a flight of steps and eviscerated several feet of intestine, which was replaced within several hours following the accident. He had a return of his symptoms and again was hospitalized. An

extraperitoneal abscess developed, which had to be incised and drained. With the aid of a transfusion and careful feeding he again made a good recovery. At the same time he complained of rectal irritation, and examination revealed several fissures and anal fistulas. These were excised.

Since that time the patient has been ambulatory. He has gained back his weight and strength, and the course was uneventful until about a month ago, when he entered the skin clinic complaining of sores on the lower parts of both legs. These were rather superficial, crusted, ulcerated lesions varying in diameter from 0.5 to 2 or 3 cm., irregular in outline and with a dirty, greenish base. The edges were not undermined. The patient stated that the lesions started as a small crusted area and broke down within a few days.

No evidence of tuberculosis was found in the chest. Roentgenographic and fluoroscopic studies gave negative results. The studies of the gastro-intestinal tract undertaken in 1931 were interpreted as showing colitis of the proximal portion of the colon with extension of the lesion into the ileum, and the possibility of intestinal tuberculosis was considered. Sections of tissue removed from the rectum showed dense granulation tissue containing large numbers of polymorphonuclear leukocytes, round cells and typical tubercles. The tubercles were composed of Langhans' giant cells, epithelioid cells and lymphocytes. Unfortunately, there was no specimen of tissue from the ileostomy opening. Biopsy on a skin lesion showed the surface epithelium in places to be atrophic. The underlying corium presented several typical tubercles, giant cell formation, epithelioid cells and a scattering of lymphocytes. Acid-fast stains of this tissue are being prepared for study. The skin cultures were unusual in that they showed Bacillus pyocyaneus in addition to the ordinary staphylococci.

The patient has been treated locally with thymol iodide and sterile dressings, with some improvement. No new lesions have appeared.

DISCUSSION

DR. D. L. SATENSTEIN: The section presented does not impress me as showing the structure of tuberculosis.

DR. L. CHARGIN: If one is to accept the histologic observations as presented by Dr. Sulzberger, tuberculosis has to be taken into consideration. On the other hand, from a purely clinical standpoint, the eruption appears to be typical of what one commonly calls pyodermia or superficial ecthyma. I believe that syphilis can be ruled out.

DR. M. B. SULZBERGER: The ulcers are superficial, shallow and covered with a yellowish crust. They are sharply demarcated, not undermined and not painful. The condition looks much like ecthyma. Biopsy on the section of the intestine revealed the same pathologic changes shown today by a section of one of the ulcers of the skin. The report on the former biopsy was that the condition was tuberculosis. It appears that neither specimen can be interpreted as showing tuberculosis.

SYPHILITIC INFILTRATION OF THE FACE SIMULATING LUPUS ERYTHEMATOSUS. Presented by DR. LOUIS CHARGIN.

This man, aged 40, an apartment superintendent, states that the cutaneous disturbance from which he is suffering appeared about eight months ago. He says that he has never had a penile lesion or lesions that could be interpreted as a secondary eruption. He also denied having suffered from gonorrhea. He was married three years ago. This was his wife's second marriage, and although she had several children with her first husband she has had none with the patient.

The eruption first appeared near the tip of the nose and has gradually spread. Now and then there has appeared a small ulceration in the affected area which has healed with the formation of a scar.

There is now marked infiltration covering the left cheek and the nose, extending to a lesser degree onto the right cheek. The eruption is in a location in which lupus erythematosus is frequently seen. The infiltrated area is irregularly outlined and at the borders shows segments of circles. There are none of the individual nodules characteristic of late syphilis. The surface of the affected area is uneven, reddish and painless and shows numerous small circular scars in the sites of former ulceration.

The Wassermann reaction of the blood was 4 plus.

DISCUSSION

DR. F. CROSS: I should think of tertiary syphilis first in this case because of the nature of the lesions. The eruption is nodular and extensive and spreads rapidly.

DR. I. M. LASHINSKY: I think that the presenter's diagnosis is good, for it is difficult to diagnose syphilis in this case. The eruption is not unilateral but somewhat symmetrical, and it greatly resembles lupus erythematosus.

DR. D. L. SATENSTEIN: The only diagnosis that can be entertained is syphilis, regardless of the distribution and of whether or not the lesions are unilateral. I came to that same conclusion before I knew the result of the Wassermann test. On close examination, one can make out distinct nodules which run together and have become confluent.

DR. L. SPIEGEL: The only diagnosis that I should make is late syphilis.

HERPES GESTATIONIS. Presented by DR. ADOLPH ROSTENBERG.

This woman, aged 26, an American, has an irrelevant family and past history. She has been married for one year and had a normal pregnancy until two days before delivery, when severe pruritus suddenly developed. An itchy, erythematous patch appeared around the umbilicus. This was diagnosed as urticaria by her physician. Two days later she was delivered of her child with the aid of low forceps. The baby was normal, and the labor was not unduly difficult or complicated. Two days after the delivery the eruption became generalized. She remained under the care of her physician for another two weeks, but the cutaneous condition grew steadily worse.

She now presents a severe eruption involving the entire body with the exception of the face. On the chest, back and abdomen there is a widespread erythematous eruption, consisting of dark red and violaceous, small and large rings with marked elevated borders, half-circles, which form gyrate figures and are interspersed with large wheals. The entire picture assumes, thus, a bizarre pattern. On the extremities, thick-set, various-sized bullae are in evidence, some of them reaching the size of a small orange. They contain a clear or sanguineous fluid. At the height of the eruption the face also became involved. The patient has had an irregular temperature, varying up to 102.5 F. The main complaint has been the intense itching. The mucous membranes are entirely free from eruption.

Examination of all internal organs gave negative results. The urine was normal except for a faint trace of albumin. Examination of fluid from the bullae revealed a total protein content of 3.83 per cent and 608 mg. of chlorides per hundred cubic centimeters of fluid. Examination of the blood showed: hemoglobin, 84 per cent; red cells, 4,460,000; white cells, 35,000; polymorphonuclears, 26 per cent; eosinophils, 53 per cent; band forms, 4 per cent; small lymphocytes, 16 per cent, and monocytes, 1 per cent.

Twenty-six days after delivery the anterior pituitary-like principle was still present in the urine. Examination of the contents of bullae for this anterior pituitary-like principle at the same time gave negative results.

DISCUSSION

DR. P. GROSS: The onset was rather late, and because of the distribution and character of the lesions I suggest a diagnosis of erythema multiforme bullosum.

DR. L. CHARGIN: Why does the presenter label the condition herpes gestationis when the eruption appeared after the termination of pregnancy? In my opinion, it is erythema multiforme bullosum.

DR. F. CROSS: There are two types of herpes gestationis: the type that begins during the later months of pregnancy and the type that starts after the birth of the child. This eruption fits into the latter category.

DR. H. SILVER: Through the courtesy of Dr. Rostenberg, I had the opportunity to observe this patient during the progress of the disease. If one assumes that herpes gestationis, which is nothing but Duhring's disease associated with pregnancy, is an entity, this eruption is a classic example of it. The severe itching, the daily crops of bullous lesions, the circinate erythematous lesions on the back and the absence of lesions of the mucous membranes leave no doubt as to the correct diagnosis. That herpes gestationis appears after pregnancy has terminated is an established fact. MacKee states that the cases of herpes gestationis that came under his observation had their onset during the puerperium.

DR. M. B. SULZBERGER: All dermatoses of the puerperium should be investigated along the lines of increase in hormones. These eruptions often do not occur during the first pregnancy but appear in succeeding ones. Therefore, there may be some sensitization basis for them. Patients with severe eruptions associated with pregnancy should be tested for deficiency of hormones.

DR. D. L. SATENSTEIN: The patient reacted favorably to her own blood. Duhring stated that this type of eruption simulates dermatitis herpetiformis in every respect except the cause, i. e., pregnancy.

DR. G. SPINNER: The patient admitted taking some drug just prior to the termination of her pregnancy. The question of drug eruption, therefore, must be considered.

DR. A. ROSTENBERG: This eruption is typical herpes gestationis, a condition first described by Milton and later studied by Duhring. Duhring described it as dermatitis herpetiformis with a known etiology. In my patient the full clinical aspect became manifest two days after the termination of her pregnancy, although a severe pruritus followed by the appearance of a bullous lesion around the umbilicus developed four days previously. This is the characteristic onset of the disease. The arrangement of the lesions also is characteristic. In erythema multiforme there is not the pronounced eosinophilia which was present in this case. The anterior pituitary-like principle usually disappears from the urine immediately after childbirth, but in this case even three weeks after her delivery there was a considerable amount present. Furthermore autohemotherapy was highly beneficial. It has been suggested that an efficacious form of therapy in these cases is the administration of the blood of a normal pregnant woman.

PITYRIASIS LICHENOIDES ET VARIOLIFORMIS ACUTA. Presented by DR. ISADORE M. LASHINSKY.

M. C., a boy aged 5½ years, presents an eruption on the face and body which began about six weeks ago. There are maculopapular lesions varying in size from that of a pinhead to that of a pea, on the trunk and extremities, and a few discrete papules on the forehead. Most of the lesions are rose-pink or red, but some are bluish. A number of lesions are topped with a tiny scale or are covered with a crust. The patient does not complain of itching. The eruption is fairly typical of pityriasis lichenoides et varioliformis acuta, but it is rather unusual to see it in such a young child.

DISCUSSION

DR. M. B. SULZBERGER: It is remarkable how many more cases of this disease are observed at the present time than formerly. The eruption is so typical that it would have been easily recognized had it occurred before. Probably it is a new entity, and one must look for new causes. This fact may offer an approach to the study of the etiology of this disease. I have seen a typical case

following an injection of a bismuth preparation and Sharlit recorded a case after injections of tuberculin. It is well that these factors are recorded, since they may give a clue to the etiology. I believe that one has here a situation similar to that in the new blood dyscrasia, agranulocytosis.

DR. D. L. SATENSTEIN: I object to the name of the disease. The lesions are not varioliform; they are rather vesicular and leave no evidence of a scar except when secondarily infected.

DR. N. PINKUS (by invitation): Jadassohn considers such eruptions as parapsoriasis en gouttes except that they are curable.

DR. P. GROSS: The remarks of Dr. Satenstein are purely theoretical, and I should accept them if he could prove his conception. In the cases that I observed typical necrosis was demonstrated histologically in some of the lesions (ARCH. DERMAT. & SYPH. **23**:33 [Jan.] 1931).

DR. I. M. LASHINSKY: The occurrence of the disease at such an early age is not common. Apropos of Dr. Sulzberger's remarks, the child was given some injections against whooping cough prior to the onset of the disease.

PARAPSORIASIS EN PLAQUES (BROCQ). Presented by DR. PAUL GROSS.

B. H., a white woman aged 26, born in Russia, presents an eruption on the extremities of nineteen years' duration.

In this location there are patches varying in size from that of a dollar to that of a palm, which are erythematous, slightly scaly and not infiltrated. Some of the lesions on the thighs show telangiectasia.

DISCUSSION

DR. L. SPIEGEL: I accept the diagnosis as presented.

DR. L. CHARGIN: I believe that the eruption belongs to the poikiloderma group. The patches are irregular, show no scaling and are telangiectatic. The distribution is not that of parapsoriasis.

DR. P. GROSS: Clinically the condition is parapsoriasis en plaques. If one observes the eruption carefully one finds that it spreads gradually. It is present now on the thighs and buttocks; it will appear on the trunk years later.

DISSEMINATED MILIARY LUPUS OF THE FACE. Presented by DR. PAUL GROSS.

This white woman, aged 40, born in Austria, presents an eruption which has been present for nine and one-half years. There has been an occasional improvement during the summer.

Both cheeks present diffuse redness and small flat or conical papules, rather uniform in character. On the right ala there is a patch of more pronounced redness, suggesting slight atrophy. The nose itself is bluish red and discolored and covered with papules similar to those on the cheeks. There are no pustules or comedones.

Quantitative tuberculin tests were negative with all dilutions. The Wassermann test of the blood was negative.

DISCUSSION

DR. M. B. SULZBERGER: Such cases are difficult to diagnose. There are no signs of rosacea. There are no ordinary acne lesions. This eruption may be a type of lupus miliaris which appears in women on the cheeks and neck and shows small papules but no signs of inflammation.

DR. A. ROSTENBERG: I have treated a patient with a similar condition with the roentgen rays with fairly good results.

A CASE FOR DIAGNOSIS (SEPTIC ULCER OF THE GROIN). Presented by DR. SAMUEL FELDMAN.

This woman, aged 25, was admitted to the Morrisania City Hospital on Feb. 2, 1934, complaining of general weakness, malaise, backache and swelling

of the legs. She is mentally retarded on account of injuries sustained at birth and is subject to epileptiform attacks. On admission she had several abrasions on her chest and admitted that they were due to picking. The temperature was 103 F. on admission and has varied from 101 to 104 F. during her stay in the hospital.

The general physical examination yielded negative results. An examination of the pelvic region also gave negative results. Roentgen examination of the chest revealed nothing abnormal, but that of the left maxillary sinus revealed a moderate cloudiness. The Widal test and the tests for paratyphoid A and paratyphoid B were negative as was also the Wassermann test of the blood. The white blood cell count has varied between 21,000 and 35,000 cells, with about 90 per cent polymorphonuclear leukocytes. The urine was found to be normal. Repeated blood cultures have been negative.

On March 1, a swelling developed in the left inguinal region. The mass soon became necrotic, and when the slough was removed there was a deep cavity reaching down to the fascia and muscles. Several small ulcerations developed about the vulva and on the buttocks. A smear from the ulcers yielded Staphylococcus aureus.

NOTE.—The patient died four days after presentation. Autopsy revealed a bacterial endocarditis.

DISCUSSION

DR. S. PECK: The ulcerated area is too cleancut. I recently saw a similar case, presented as one of syphilis, in which the lesions rapidly became necrotic and did not respond to antisyphilitic therapy. This patient's condition may be a Schwartzman phenomenon, which is a toxic reaction due to vascular destruction of a staphylococcus or a streptococcus.

JUXTA-ARTICULAR NODES. Presented by DR. SAMUEL FELDMAN.

This woman, aged 55, states that the duration of her condition is about ten years. She was unaware of the nature of the disease and attended clinics for many years, where she received topical applications. She has never received any antisyphilitic treatment.

On the right upper arm and forearm, in the vicinity of the elbow, there are a number of irregular scars and copper-colored papules, grouped about the scars or in clear areas, which present a serpiginous outline. On the forearm, just below the elbow joint, there are three nodules ranging in size from that of a pea to that of a large bean, arranged in a row. They are firm to the touch and move freely with the skin. Serpiginous tertiary syphilitic lesions and scars are present in the region of the right knee. Here, also, there are three small nodules which are arranged in a row and are located close to the knee joint.

TINEA CAPITIS (THREE RECURRENCES AFTER TREATMENT) AND TRICHOPHYTIDS. Presented by DR. ARTHUR SAYER.

This colored boy, aged 8 years, born in the United States, first appeared at the Mount Sinai Hospital on Aug. 27, 1929, because of an eruption on the scalp. The scalp then presented scattered areas of scaliness and partial alopecia. An examination for fungi gave positive results. He was then given 0.127 Gm. of thallium acetate (his weight was 35 pounds [15.9 Kg.]), which resulted in fairly good epilation of the scalp. He was subsequently given sulphur ointment to be applied locally, and the clinical result was an apparent cure.

He presented himself again on April 5, 1932, and at that time he again showed scattered areas of scaliness and partial alopecia of the scalp and diffusely scattered small papular and papulovesicular lesions on the neck, trunk and upper extremities. The microscopic examination for fungi gave positive results. He was referred to the roentgen therapy department for roentgen epilation of the scalp. The epilation was successful, and the hair regrew in about three months, with no apparent

recurrence of the tinea. He returned on May 10, 1933, with several small patches of alopecia and scaliness of the scalp and an acute exacerbation of the eruption on the neck and trunk (trichophytid). Examination for fungi was reported as arousing suspicion of tinea.

He came back to the clinic on March 8, 1934, with a diffusely scattered pustular and crusted eruption on the scalp which looked not like the previous eruption but more like impetigo. He also had an eruption on the neck, chest and back, consisting of small papular and erythematous scaly lesions which looked more like chronic eczema than like trichophytid.

DISCUSSION

DR. C. WOLF: I did not agree with the diagnosis when I saw the child at Mount Sinai Hospital. A third infection is rather unusual. Not often does one see such a case.

DR. F. CROSS: I should say that the condition of the scalp was not entirely cleared up rather than that the scalp was reinfected.

DR. M. B. SULZBERGER: I should like to have permission to make trichophyton tests on this child. The condition is probably very refractory.

DR. D. L. SATENSTEIN: Not only the treatment of the patient but his environment is important. I do not believe that one can build up immunity in such cases.

DR. A. SAYER: The members must agree that this case is extremely unusual. Microscopic examination showed ordinary Microsporon.

HENRY SILVER, M.D., *Secretary*

Regular Meeting, April 26, 1934

SAMUEL FELDMAN, M.D., *President*

GENERALIZED SCLERODERMA. Presented by DR. CHARLES WOLF.

This colored woman, aged 38, a seamstress, states that two years ago she noticed stiffness and tightness in her ankles and knees. This was followed by swelling which extended up to the knees. Her hands and arms and finally her face became similarly involved. The patient then noticed a waxy shininess of the skin. For eight months she has been totally incapacitated because of the stiffness of her joints. Four or five months ago the swelling disappeared, and since then she has presented the picture now seen.

The entire integument has a waxy-looking, smooth, glistening, stretched appearance. The face is expressionless and masklike. The skin is taut and indurated. The nose is pinched. The skin covering the articulations is sclerotic and tense, restricting the motions of the joints so as to cause inability to bend or move the fingers, wrists, elbows and shoulders. The deeper tissues are implicated, as evidenced by atrophy of the underlying muscles and subcutaneous tissues. The bones are involved, as shown by roentgen examination. There are areas of hyperpigmentation all over the body, particularly on the face. The soles, palms, mucous membranes of the mouth and vagina are excluded from this generalized process.

The temperature has been normal at all times. There have been no previous major illnesses. The patient has not menstruated for two years.

The blood count revealed: white cells, 14,000; red cells, 4,100,000; polymorphonuclears, 65 per cent; hemoglobin, 80 per cent. Roentgen examination of the skull gave negative results. The bones of the hands and feet showed marked decalcification with narrowing. Urinalysis revealed nothing abnormal. A search for arsenic yielded none.

The section showed a markedly pigmented epidermis. Most of the pigment was in the basal layer. There was a moderate amount of inflammatory reaction

in the upper part of the cutis, especially in the papillae, consisting mainly of mononuclear cells in strands. The character of the fibers in the cutis did not seem to be changed to any degree. The appendages appeared normal. A diagnosis of scleroderma could not be made from this section with the hematoxylin-eosin stain.

Therapy was begun on March 29 with thyroid extract, 1 grain (0.06 Gm.) three times a day. The patient has also received sodium thiosulphate, 15 grains (0.96 Gm.) three times a day, cod liver oil with viosterol, 1 teaspoonful (4 cc.) three times a day, and calcium gluconate.

For a week the patient has been able to move the skin of her face so as to smile and furrow her forehead. She has been able to move her finger joints and has slight movement in her elbows and shoulders. Her skin has been exfoliating and is softer.

DISCUSSION

DR. M. B. SULZBERGER: I agree with the presenter that the condition is generalized scleroderma. It is interesting to see it in a colored person. I should like to know the incidence of this disease in Negroes.

DR. A. ROSTENBERG: I have seen several cases of scleroderma in colored people. This patient is responding well to treatment, and I think that the most important factor in the therapy of this disease is rest. Extract of pancreas has been reported to be a good therapeutic agent. However, that has not been my experience.

DR. D. L. SATENSTEIN: Though the face is fixed, on palpation of the skin it felt soft. I cannot accept the diagnosis of scleroderma. Furthermore, the biopsy did not definitely prove the condition to be scleroderma.

DR. W. SACHS: I venture a diagnosis of dermatomyositis. I saw a similar case at the Mount Sinai Hospital. In that case there was pain in addition to the swelling.

DR. L. CHARGIN: I hesitate to make a definite diagnosis but suggest scleredema adultorum (Buschke). There was an acute onset, and the process became generalized. The skin lacks the hard character of scleroderma. The pigmentation must be discounted, especially since the patient is colored. There is definite pitting on the forearms, which is not found in scleroderma. There is not enough pain to justify a diagnosis of dermatomyositis. Buschke's scleredema, therefore, is the most likely diagnosis.

DR. L. SPIEGEL: I accept the diagnosis as presented.

DR. S. PECK: One cannot argue against dermatomyositis. The disease is not uniform in symptomatology. There are marked pitting and pain on pressure.

DR. S. FELDMAN: There has been little change in the condition since I saw the patient six weeks ago. There has not been extreme hardness at any time.

DR. C. WOLF: The so-called depigmentation is normal skin. The patient was very fair and the darker color is abnormal pigmentation. The condition began with severe pains in the joints, which is the usual manner of onset of scleroderma. When I first saw the patient four weeks ago the skin was hidebound. She did not have the intense desquamation that is evident now. I also considered an avitaminosis and administered viosterol and cod liver oil.

GENERALIZED MONILIASIS AND MONILIIDS? Presented by DR. MARION B. SULZBERGER for DR. H. PINKUS.

M. S., a white girl 16 years of age, is a patient in the Montefiore Hospital because of chronic glomerulonephritis. She had had two attacks of pneumonia, bilateral parotitis (after the administration of iodides) and a suppuration of the glands of the right side of the neck, which were incised.

The cutaneous condition began three years ago. It has been characterized by recurrent, generalized attacks of papular, pustular and eczematous lesions accom-

panied by high temperature. Three weeks ago an acute dermatitis of the face developed a few days after exposure to the sun.

The eruption now involves the scalp, face, corners of the mouth, inguinal region and toes.

The patient gave a positive reaction to oidiomycin and to trichophytin.

DISCUSSION

DR. M. B. SULZBERGER: The eruption was much more widespread when the patient was first seen two years ago. The clinical picture was that of a macerated condition of the fingers and toes, weeping seborrhea-like lesions on and behind the ears, perlèche and crusting and scaling of the scalp. This resembled the cases of moniliasis that I have seen. Further confirmatory evidence is that the patient was highly sensitive to an injection of Monilia extract. The condition has been refractory to treatment, which also speaks in favor of moniliasis.

DR. W. SACHS: From Dr. Sulzberger's description I should say that the patient has moniliasis, although from the appearance of the lesions tonight I should hesitate to make that diagnosis.

DR. S. PECK: Reactions to trichophytin are practically valueless in adults, but the younger the person (below 12 years of age) the greater the significance of a positive trichophyton test. The same thing may be said with regard to oidiomycin.

DR. A. SAYER: Special dietary regimens have been recommended for such refractory patients. I have seen no benefit from them, and I think that diet is overstressed.

DR. C. LERNER: The case should be studied from an internal medical standpoint, especially from the gastro-intestinal standpoint. Hopkins reported the isolation of Monilia from the intestines in one case.

DR. M. B. SUZLBERGER: It would be difficult to make a diagnosis of moniliasis as the condition appears tonight. I cannot be sure that Monilia is the true etiologic factor. The patient has many internal manifestations that may or may not be those of moniliasis. There is a characteristic facies which this patient presents. If the condition is not moniliasis, what is it?

DR. C. GREENHOUSE: There have been many cases of Vincent's disease which produced manifestations in the lungs. Why cannot cases of moniliasis show similar pulmonary findings?

DR. S. FELDMAN: Many cases that go under the diagnosis of tuberculosis of the lung are really due to various fungi such as Monilia, Trichophyton, Aspergillus and Penicillium.

MULTIPLE PIGMENTED HEMORRHAGIC SARCOMA OF KAPOSI. Presented by DR. GEORGE J. SPINNER.

This man, aged 67, apparently in good health, gives irrelevant past and family histories. About six months ago he began to feel an irritation behind his right ear and soon noticed several small nodules. Within a month similar nodules appeared below his right elbow, accompanied by mild pruritus.

The lesions are now disseminated over various parts of the body and are beginning to appear on the chest. They are small, elevated, bluish-black, firm nodules ranging in size from that of a lentil to that of a split pea.

The Wassermann reaction of the blood was negative. Histologic examination revealed the typical structure of Kaposi's sarcoma.

DISCUSSION

DR. D. L. SATENSTEIN: This is an interesting and typical case of Kaposi's sarcoma, but the lesions have an unusual distribution.

DR. L. CHARGIN: The onset on the ear is unusual, but such an onset has been recorded previously.

RECKLINGHAUSEN'S DISEASE IN FOUR MEMBERS OF ONE FAMILY. Presented by DR. CHARLES LERNER.

Mrs. R. S., aged 36, a Jewess, born in the United States, came to the dermatologic clinic of the New York Post-Graduate Medical School and Hospital with her two children, all presenting similar eruptions. She states that some of the lesions have been present since birth.

An inquiry into the family history revealed that the patient's father had multiple soft tumors distributed over his body. She had four brothers and sisters. One died in infancy; one is supposedly normal; one died at the age of 16 of a tumor of the brain (Recklinghausen's disease?), and a brother, seen at the clinic, has advanced lesions of Recklinghausen's disease associated with osseous changes. Her husband gave a history of a "lump" on the arm which recurred following excision. Of her four children (third generation) only one is apparently free from the disease. Two are presented here, while the third child is said to have a soft tumor on the labium majus pudendi.

There are many café au lait macules on the mother's trunk and extremities, as well as slightly elevated brownish spots and soft pendulous pea-sized to prune-sized tumors which can be invaginated. The patient also has an ankylosis of the left upper radio-ulnar articulation and a right dorsal scoliosis.

The son, aged 13, presents cutaneous lesions similar to those of his mother, but in greater number. There are also two corrugated, pigmented lesions resembling large nevi. One involves the nape of the neck, right shoulder and interscapular region; the other, the left elbow joint. There are scars on the head left by the surgical removal of tumors.

The daughter, aged 9, presents several café au lait spots and a few brownish, slightly elevated, coin-sized lesions on her trunk and extremities. The eruption is apparently of the forme fruste type.

DISCUSSION

DR. M. UMANSKY: One of the patients presents a nevus anaemicus, which of course is known to exist in association with Recklinghausen's disease.

DR. T. ROSENTHAL: This is a very good example of a genodermatosis. Tumors of the spinal cord are often found in such cases. Removal of tumors often results in recurrence.

DR. A. SAYER: It is interesting to observe that in rare instances such tumors may become malignant. I recently encountered an example of this.

DR. C. LERNER: Recklinghausen's disease is usually associated with disturbance of the endocrine system. The patient sometimes has a physical as well as a mental imbalance. Surgical removal is employed only when the tumors are large, when there is danger of infection or when they interfere with locomotion, and also when only a few are present. They originate from the perineurium and are subcutaneous.

LUPUS ERYTHEMATOSUS DISSEMINATUS. Presented by DR. SAMUEL FELDMAN.

Miss B., aged 23, a school teacher, noticed about three years ago two red, scaling patches on the face; they soon assumed a butterfly appearance. The diagnosis of lupus erythematosus was established, and treatment with gold sodium thiosulphate was instituted. After the second injection there developed high fever, general malaise, a sore throat and swelling of the cervical glands. The reaction was of short duration, and the treatments were continued in spite of it. The eruption disappeared within a few months.

About one year ago the condition recurred. There was a new patch over the eyelid, and several areas on the backs of the fingers were involved. Gold sodium thiosulphate was again given. A severe reaction followed the second injection. It began with fever, sore throat and pain and swelling of the glands in the neck and culminated in a general macular eruption, resembling measles. The patient

was treated with sodium thiosulphate, and the reaction gradually subsided. It is evident, however, that the disease has made considerable progress. Large patches of typical lupus erythematosus have appeared on each cheek occupying almost the entire face, and many smaller patches have appeared on the dorsal surfaces of the fingers, hands, wrists and forearms.

Some patches present dilated follicular openings with adherent scales. There are several areas of atrophy.

NOTE.—Subsequent to presentation, the patient received 5 grains (0.3 Gm.) of quinine sulphate and there immediately developed a reaction similar to that following the injections of the gold compound.

DISCUSSION

DR. S. FELDMAN: Treatment occasionally aggravates lupus erythematosus. What shall one do for a patient who is susceptible to gold compounds, as this woman is?

DR. L. CHARGIN: Even when one is successful in the treatment of this disease with gold compounds, there is often a relapse. The eruption that appears after injections of a gold compound is not lupus erythematosus but a form of multiform erythema, even though clinically the conditions resemble each other. Thus the gold compound does not stimulate the formation of new lupus erythematosus lesions but rather causes toxic manifestations. Silver arsphenamine may be tried.

DR. D. L. SATENSTEIN: Following ultraviolet irradiation lesions develop that resemble acute disseminated lupus erythematosus, but I feel that these lesions are not the same but a toxic reaction. The mechanism of the production of such lesions is not known. I think that the old-fashioned treatment with trichloracetic acid is good and is being neglected.

DR. S. PECK: A salt-free diet as well as injections of a bismuth preparation should be tried.

DR. M. B. SULZBERGER: I should like to add plasmochin to the armamentarium for the treatment of this disease. It was used with considerable success in European clinics. It is occasionally dangerous.

DR. H. SILVER: Plasmochin was first introduced by Buschke for the treatment of pemphigus. I have tried it, but the results were not gratifying. I caution against too great optimism in the use of this drug.

DR. S. FELDMAN: The eruption is present on the exposed portions of the body, tending to show a photosensitization. There is no question that the lesions on the fingers are lupus erythematosus, and these were present even before the reaction. Thus I believe that the entire process is an extension of the lupus erythematosus and not a toxic phenomenon.

A CHARCOT JOINT. Presented by DR. ARTHUR SAYER.

P. G., a colored (mixed Indian and Negro) man aged 54, born in the United States, presented himself at the Morrisania Hospital in December 1933 on account of swelling and deformity of the left ankle which he stated had existed for four years.

He gives a history of having had a penile lesion about thirty years ago. He was not treated until 1930, when he received about twenty intravenous and twenty intramuscular injections at a Philadelphia hospital.

The left ankle shows diffuse swelling, but there is fair motion in all directions. It is approximately twice the size of the right ankle. It is only slightly painful and slightly tender. He is able to walk on it without much discomfort.

A roentgenogram of the left ankle showed extensive destruction and fragmentation of the bones of the ankle joints and of the tarsal bones, disorganization of practically all the joints and swelling of the overlying soft parts. The appearance was that of a trophic destruction.

The Wassermann reaction of the blood with alcohol and cholesterol antigens was negative. The Kahn reaction was also negative.

The patient has been given antisyphilitic treatment for three months with practically no effect on the ankle joint.

NEW YORK DERMATOLOGICAL SOCIETY

R. H. RULISON, M.D., *Secretary*

Regular Meeting, March 27, 1934

EDWARD R. MALONEY, M.D., *President*

XANTHOMA TUBEROSUM MULTIPLEX IN A CHILD AGED TWO AND ONE-HALF YEARS. Presented by DR. FRED WISE.

This white girl, aged 2½ years, from the New York Post-Graduate Medical School and Hospital, has an eruption which first appeared six months ago. The child is apparently in robust health and well nourished. There are no subjective symptoms. The family and personal histories are unimportant.

The lesions are typical lemon-yellow to reddish-yellow nodular formations located mainly in the intergluteal cleft, just over the coccyx, on the back of each hand, in the popliteal areas and over the achilles tendon of each foot, about an inch (2.5 cm.) above the plantar surface of the heel. The lesion at the base of the spine is 1½ inches (3.7 cm.) long and ½ inch (1.2 cm.) broad. The lesions over the achilles tendons are hemispheric, hard nodules, about the size of a large French pea. Those on the hands vary in size from that of a barleycorn to that of a lentil and are flattened papules.

There has not been time for laboratory investigations.

DISCUSSION

DR. H. H. WHITEHOUSE: I do not know that I have ever seen such a case in a child of this age. I think that the patient's age is the unusual feature.

DR. HOWARD FOX: I have published a photograph of this type of xanthoma in a child about 4 years old. This condition is certainly rare in children.

DR. FRED WISE: Urbach, of Vienna, in his recent book cites references to cases of xanthoma multiplex cured by a cholesterol-poor and fat-free diet.

DR. HOWARD FOX: Udo Wile, I believe, caused improvement in some of his cases by a fat-free diet.

MULTIPLE GIANT CELL SARCOMA: BENIGN TYPE. Presented by DR. HOWARD FOX.

This woman, aged 40, born in Italy, a waitress, first noticed an eruption twenty-eight months ago. It began on the fingers and has gradually increased in extent until it involves the hands, elbows and bridge of the nose. The eruption is chiefly on the hands, where the lesions are subcutaneous, pea-sized nodules, not attached to the overlying skin. Some of them are attached to the underlying tissues, and a few are freely movable on them. The lesions over the last phalanges of the fingers are more closely attached to the skin and are somewhat reddish and in places scaly. Other lesions of the hands and fingers are flesh-colored or bluish. The lesions are somewhat tender to the touch. Some are soft, and others are as hard as cartilage. There are, roughly, about eighty lesions on the hands and fingers. On the elbows there are a few soft, pea-sized, purplish nodules. On the bridge of the nose are a few extremely hard, slightly elevated lesions. On the

forehead are numerous elevations the size of a small pinhead which are totally unlike the rest of the eruption.

The patient is rather small and slim and in good general health. She has one child, now aged 21, and had one miscarriage two years after the birth of this child. In 1926 she underwent a salpingo-oophorectomy, which was followed by cessation of the menses.

A nodule was excised from a finger and was examined histologically by Dr. T. J. Riordan, who reported as follows: "There are an unusual number of foreign body giant cells, some small, others large, with nuclei arranged concentrically or in horseshoe fashion. There is proliferation of blood vessels. The process is one of giant cell reaction. Both calcinosis and xanthoma can be excluded."

DISCUSSION

DR. J. FRANK FRASER: My first impression from the gross appearance of the lesions was that they were so-called synovial lesions, but the histologic picture excludes that diagnosis. On looking at the slide I was impressed with the resemblance to giant cell sarcoma, especially the type which arises from the alveolar process of the jaw bone, commonly known as epulis. The histologic picture here is exactly similar to the picture in that condition. I think that this condition should be classified as a benign so-called giant cell sarcoma of the epulis type, which arises from the periosteal or endosteal lining of bone. Such tumors do not metastasize and when thoroughly removed do not recur.

DR. GEORGE M. MACKEE: The case is interesting because of the large number of lesions scattered over the hands and face, ranging from papules the size of a pinhead or even smaller to nodules the size of a pea. The histopathologic picture is particularly interesting because it is that of a giant cell tumor. I suspect that the condition is that which used to be called "giant cell sarcoma of the skin," but which is not a true sarcoma and is not malignant. Years ago I treated several apparently similar growths successfully with the roentgen rays. The lesions were on the scalp, and they were very radiosensitive. I suggest that this patient secure such treatment, each lesion being given from 2 to 4 skin units (from 560 to 2,400 roentgens) of unfiltered radiation.

DR. H. H. WHITEHOUSE: Dr. Fraser has described the pathologic process, and I should like to ask him whether he can tell from this slide whether the growth seems to have developed from the periosteum of the bone. Or is his statement that such growths often develop from the periosteum? Did the process develop from the periosteum in this particular case? I had in mind clinically the possibility of a Darier-Roussy sarcoid, which is not entirely ruled out by the histologic findings. I think that it is possible that these giant cells are the giant cells of that disease. The giant cells are a very prominent feature in that type of sarcoid. Whether there are any inflammatory features resembling tuberculosis, I do not know.

DR. J. FRANK FRASER: One would not be able to say from a study of this slide that the tumors arose from the periosteum. What I meant to say was that they looked exactly like tumors which I know do arise from that tissue.

DR. GEORGE M. MACKEE: Are these lesions sarcomas? If they are not sarcomas, are they neoplasms? Are they benign or malignant? Is this the type of lesion that was known as a cutaneous giant cell sarcoma twenty years ago but which is now thought to be simply a benign local reaction with giant cell formation? Perhaps Dr. Fraser can answer these questions.

DR. HOWARD FOX: When I first saw the patient I naturally thought of cutaneous calcinosis and xanthoma, though I was not entirely satisfied with either diagnosis. Clinically the case was unique, and this has been borne out by the histologic examination. I am unaware of the nature of the tiny lesions on the forehead and shall try to obtain tissue from one of them for study. I do not know whether they have any relationship to the lesions on the hands. I am

pleased to hear of the possibility that these tumors may be radiosensitive and shall treat some of them with the roentgen rays.

DR. J. FRANK FRASER: There is a giant cell tumor that is neoplastic, but the cells are not the same type of giant cells as those in this case. They are more like the myelogenous giant cells. These are more like the foreign body giant cells. These lesions are the type of tumors that would formerly have been called giant cell sarcomas of the skin.

ONYCHOMYCOSIS AFFECTING ALL NAILS OF THE FINGERS AND TOES. Presented by DR. HOWARD FOX.

This man, aged 43, born in Italy, a presser, was referred from Veterans Hospital No. 81 for diagnosis of a disease of the nails which has existed for six years. All of the nails of the fingers and toes are abnormal, the changes in all of them being similar and affecting especially the distal halves. The nails are lusterless and yellowish and show marked onychauxis of the distal ends, a few pinpoint pits and longitudinal striae. There is no paronychia and no appreciable eruption of the skin of the fingers or toes. After diligent search, a fungus was demonstrated microscopically by preparations in potassium hydrate of scrapings from both finger-nails and toe-nails. Unmistakable septate hyphae were found. Cultures were made, but too recently for an opinion to be available. The patient states that a fungus was demonstrated in the finger-nails two years ago. In addition to the disease of the nails, there is a diffuse, scaly thickening of the palms which has been present, according to the patient's statement, since 1917.

DISCUSSION

DR. GEORGE M. MACKEE: The case is particularly interesting because it is unusual to have every nail involved. I have observed several such cases in which the diagnosis was made clinically and only one in which the diagnosis was confirmed by microscopic examination and cultures.

DR. HOWARD FOX: Ringworm of all of the nails of the fingers and toes is unusual. In an excellent monograph to be published shortly by Pardo Castello, mention is made of this fact and a few cases are cited, one of them reported by Dr. MacKee and one by Dr. Wise.

GENERALIZED PROGRESSIVE SCLERODERMA. Presented by DR. HOWARD FOX.

This man, aged 33, born in the United States, a glass-blower, was referred from the Veterans Hospital in Lyons, N. J., because of an eruption which has been present for five years. He shows hidebound skin to a marked degree on the face, trunk and upper extremities, and to a lesser degree on the lower extremities. The hands are only moderately affected. The skin is otherwise normal, with no pigmentation. Following wounds from high explosives during the World War the patient has been mentally deranged; he attempted suicide on one occasion. He is said to have a piece of shrapnel near the base of the brain at the present time. He is of medium size and weight. The urine showed a trace of albumin, and a blood count showed 12,600 leukocytes. The patient's failure to cooperate properly has made it impossible to perform a basal metabolism test.

DISCUSSION

DR. BINFORD THRONE: The patient should be investigated for the possibility of retention of arsenic.

DR. FRED WISE: Does Dr. Fox think that this is the type of case which if it progresses is liable to cause asphyxiation because of immobilization of the diaphragm? I saw one such case in the Vanderbilt Clinic in which the entire chest became hardened and the man became cyanotic and nearly died because of inability to get oxygen into the lungs.

Dr. Howard Fox: I consider this to be the progressive type of scleroderma which will gradually become worse and in which treatment will probably be of no avail. It differs from the usual case in that the hands are only slightly affected.

Rosacea-Like Tuberculid of Lewandowsky. Presented by Dr. George M. MacKee.

This article will appear in full in a later issue of the Archives.

Sarcoma of Kaposi in a Woman. Presented by Dr. Howard Fox.

M. J., aged 39, a married woman, first noticed an eruption on her legs one year ago. She now presents about fifteen nodules varying in size from that of a millet seed to that of a large pea on the posterior and lateral aspects of the lower half of each leg. There is also one pea-sized nodule on the left sole. The lesions are discrete, firm, elevated and sessile. The majority show some scaling but not scratch marks. Some of the lesions are bluish red. The histologic report is not ready.

Multiple Hemorrhagic Sarcoma of Kaposi. Presented by Dr. Fred Wise.

This man, an Italian, a gentile, aged 62, from the clinic of the New York Post-Graduate Medical School and Hospital, has an eruption which appeared fourteen years ago. There are nodular and papular, brownish-black, violaceous and reddish-brown infiltrated lesions, not tender to pressure, situated mainly on the dorsa of the hands and fingers, with flat violaceous lesions on the palms. The anterior surfaces of both legs and thighs exhibit similar multicolored nodular lesions varying in size from that of a lentil to that of a large pea. On the dorsa of the feet the lesions are much larger, confluent, elevated and darker. On the lateral and dorsal surfaces of the toes, the appearance is that of a chronic verrucous process. The soles exhibit confluent, elevated, dark brown and violaceous plaques, of irregular outline.

The left side of the neck presents a moderate degree of adenopathy, the glands being soft to the touch. The patient complains of pain in the feet and legs. His general health has begun to deteriorate in the past year. He is to be admitted to the hospital for examination and for treatments with filtered x-rays.

DISCUSSION

Dr. Fred Wise: Two years ago I presented before this society a woman with Kaposi's sarcoma whose body was riddled with tumors. She was from the New York Post-Graduate Medical School and Hospital. She never responded to any treatment, either with filtered or with unfiltered x-rays or with arsenic.

Dr. Paul E. Bechet: Does Dr. Fox know what the relative frequency of the disease is in men and in women?

Dr. Howard Fox: I cannot answer Dr. Bechet's question and should like to know myself the exact proportions of males and females affected. For the moment, I can recall seeing only one other woman with Kaposi's sarcoma. I am convinced that this is a racial disease, an opinion which is more or less generally held.

Dr. George M. MacKee: Does any one know whether patients ever die of Kaposi's sarcoma?

Dr. Fred Wise: In some cases of Kaposi's sarcoma, death results from malignant spindle cell sarcoma of the viscera or of the skin.

Dr. J. Frank Fraser: Dr. Wise's statement that patients do not die of Kaposi's sarcoma is in accord with the views of the English pathologists who claim that Kaposi's sarcoma should not be classified with the sarcomas, that it is an inflammatory process. Sequeira mentions in his latest textbook that those patients who died do so as a result of a malignant sarcoma which histologically

is not at all like Kaposi's sarcoma of the skin. As Dr. Wise mentioned, the malignant sarcomas of the viscera are of the spindle cell type. I have studied some early lesions of the skin carefully, and all one sees is proliferation of capillary endothelium without any histologic signs of malignancy.

DR. FRED WISE: The textbooks say that the disease is much more prevalent in Jews than in gentiles, a statement which I have never been able to satisfy myself was true. It is probably true with reference to New York.

DR. GEORGE M. MACKEE: It does seem in this city, at least, that this disease is seen more frequently in Jews.

DR. BINFORD THRONE: It seems to me that I have seen a large number of cases in Italians; there are of course many in Jews, but Italians certainly add their quota. They were not Italian Jews either.

DR. H. H. WHITEHOUSE: My opinion is the same as that expressed by Dr. MacKee. Almost all of such cases seem to be in Jews.

DR. RAY H. RULISON: Dr. Highman used to insist that there were certain diseases that were supposed to be racial but that were really geographic, and that Kaposi's sarcoma could be classified as a Mediterranean disease. However, as far as my recollection goes, a high percentage of the patients come from northern Europe. The condition cannot be classed as a Mediterranean disease unless one goes back in the patients' ancestry and considers that the Polish and Russian Jews originated in Palestine.

DR. E. R. MALONEY: From my experience, I feel that Kaposi's sarcoma is a disease which is found generally among Jews, but that one sees a fairly large number of cases in gentiles.

ACHROMIA PARASITARIA? Presented by DR. FRED WISE.

This Negro, aged 33, born in the United States, from the clinic of the New York Post-Graduate Medical School and Hospital, gives a history of having had a penile lesion in 1917, which disappeared after local therapy. He denies having had syphilis. The result of the Wassermann test has not been reported.

The eruption is of two years' duration and consists of spots of relative depigmentation scattered over the face and trunk. Those on the face vary in diameter from ¼ to ½ inch (0.6 to 1.2 cm.) and are discoid and free from scales or other surface changes, except that their color is a light tan, as contrasted with the surrounding dark skin. There are approximately thirty such areas on the face. On the trunk and upper extremities a few similar lesions exist, which vary from ½ to 1 inch (1.2 to 2.5 cm.) in diameter. On the right side of the abdomen is a depigmented area about 2 inches (5 cm.) in diameter, with irregular edges, which closely resembles a nevus anaemicus; the patient states that this depigmented area had been present since birth. On the arms there were several dime-sized areas with active superficial adherent scales.

DISCUSSION

DR. HOWARD FOX: A number of years ago I reported cases from Harlem Hospital as instances of partial depigmentation of the face occurring especially in colored children. Later, Dr. Pardo Castello, with the help of a bacteriologist, published his article entitled "Achromia Parasitaria," describing precisely the same condition. Similar cases have been described in various parts of the world, and in my opinion the condition is common in dark-skinned races, especially in the tropics. The name "achromia" is not quite correct, as this signifies complete depigmentation, whereas the depigmentation is only partial. As Dr. Pardo Castello admitted, the presence of fungi, especially Aspergillus, in the minority of his cases is not positive proof that the disease is caused by fungi. Treatment has certainly been unsatisfactory in my experience. I have always thought it possible that these cases might be due to streptococci as well as to fungi as Dr. Wise suggested. I

also think that while the disease is probably more common in the colored races the impression of frequency of the disease may be due to the contrast of the light patches on the dark skin.

Dr. Binford Throne: The only thing I was thinking about here was the term "achromia parasitaria." Is that used in contradistinction to the term "achromia postparasitaria," which has been applied to the conditions which one sees frequently over the sites of a preexisting tinea versicolor?

Dr. George M. MacKee: I agree with what Dr. Fox said, and I think a better name for this condition is something like "achromia partialis circumscripta."

Dr. Fred Wise: It is true, as Dr. Fox said, that the condition is common in Mexico and the tropics. All dermatologists have seen many such cases there, but in this city a Negro who applies for treatment at the clinic for this condition must have it in such an advanced and conspicuous form that it attracts not only his attention but the attention of others. Evidently the condition is not so common in adults in this city as it is in children, and it is not very common in children in the North.

Erythema Toxicum (Following the Application of Resinol Ointment?). Presented by Dr. Fred Wise.

This man, aged 51, from the clinic of the New York Post-Graduate Medical School and Hospital is in good general health, and his family and personal histories are unimportant.

He states that he sprained his right ankle several weeks ago and that adhesive plaster was applied to it. On removal of the plaster, a denuded area of skin appeared on the ankle and sole of the affected foot. To this dermatitis he applied resinol salve one week ago. Twenty-four hours after the application of the salve to the foot, a rash appeared on the legs, thighs, backs of the hands, upper extremities and axillary spaces, extending to the shoulders. The eruption consists of reddish to purplish, discoid, macular plaques, some of which are slightly edematous and elevated; it is most pronounced on the dorsa of the hands and the extensor surfaces of the forearms and arms. On the anterior surfaces of both legs, there are well defined discoid purpuric plaques, varying in size from that of a pinhead to that of a dime. The patient complains of burning of the skin, but no itching. Patch tests with resorcinol were made today, too recently for a report to be available.

DISCUSSION

Dr. Paul E. Bechet: The eruption resembles erythema multiforme of an urticarial type. I do not believe that it is due to resinol ointment. I think that Dr. Wise will find that the patch test will be negative, and that the condition is urticaria and not dermatitis venenata.

Dr. Binford Throne: I think that the eruption is erythema multiforme, but the relationship to the resinol ointment or to any of its components remains to be proved.

Dr. Howard Fox: Clinically the condition is merely erythema multiforme associated with purpura, which one frequently sees. I was interested in Dr. Wise's suggestion of possible absorption of resinol through broken skin with the production of a general eruption. Resinol, from my experience, can certainly produce irritation in sensitive persons. This case may be similar to those in which a generalized eruption appears following the local use of a belladonna plaster.

Pemphigoid Eruption in an Infant. Dr. Howard Fox.

A child, aged 10 months, was presented before this society on Feb. 27, 1934. I saw him this morning. He shows great improvement, although there have been several fresh crops of vesicles and bullae arising on normal skin. His general

condition seems to be excellent. I still think that he has a pemphigoid eruption which will prove to be benign. I do not think the eruption is true pemphigus.

DISCUSSION

DR. FRED WISE: The only thing I have to add is that a blood count was made, and that the white cell count was 18,200, with 28 per cent eosinophils. On the strength of the eosinophilia and of observations of the lesions as they developed, a tentative diagnosis of Duhring's disease was made. The child was given a preparation of plasmochin, which is used in the treatment of malaria. The iodide test was made and gave negative results. Fresh crops of lesions are still appearing, so I do not think that much has been accomplished, but the skin has greatly improved.

MANHATTAN DERMATOLOGIC SOCIETY

MIHRAN B. PAROUNAGIAN, M.D., *Secretary*

April 10, 1934

FRED WISE, M.D., *Chairman*

XERODERMA PIGMENTOSUM. Presented by DR. JOSEPH J. ELLER.

This Jewish boy, aged 4½ years, has the following history: At the age of 6 weeks he was exposed to the sun for one hour. Following this his mother noticed a gradually increasing pigmentation and freckling involving the skin of the face, neck, hands and legs. The pigmentation progressed, and during its course keratoses developed and then ulcerations. Squamous and basal cell epitheliomas have been removed from the patient's face at various times. The boy has been kept out of the sun, but the condition has continued to progress.

He now presents numerous keratoses, ulcerations and fungoid epitheliomas involving the face and marked infiltration of various portions of the face, especially the upper lip.

DISCUSSION

DR. LUDWIG OULMANN: This is certainly a sad case. I do not think that much can be done.

DR. MAX SCHEER: Has roentgen therapy been employed?

DR. FRED WISE: I suggest excision with electrocoagulation and treatment with roentgen rays or with radium. I do not think that such cases are always fatal.

DR. JOSEPH J. ELLER: The parents have been instructed to keep the child away from sunlight. He has had from thirty to forty tumors extirpated with the electric cutting current, but there have been recurrences. The extirpation was not followed by treatment with roentgen rays or with radium.

TUBERCULOSIS OF THE HYPODERM. Presented by DR. JOSEPH J. ELLER.

Mrs. A. J. on Sept. 6, 1933, had a tooth devitalized. Three weeks later, on September 27, an inlay was introduced. The patient states that she felt a burning pain while the inlay was being cemented into place. The pain lasted for about two hours. At that time she first noticed a small, hard lump immediately below the medial half of the zygoma. The mass continued to increase in size. The tooth was extracted on October 11, but the growth continued to increase slowly in size. On November 6 (ten days after the onset of the lesion) the patient was referred to a surgeon specializing in operations on the mouth for excision of the growth. Following the operation the entire side of the face swelled considerably. The

swelling subsided in a week, but at that time the patient noticed that the hard mass had already recurred. Complete roentgen examination of the mouth failed to reveal any abnormality. On November 20 another tooth was extracted, and the recurrent growth was again removed.

General examination revealed nothing abnormal except a small, firm subcutaneous tumor the size of a hickory-nut which seemed to be attached to the interior median border of the left zygoma. The skin of the left cheek was normal. There were no lesions of the mucous membrane.

The patient gave positive reactions to tuberculin in dilutions of 1:100,000 and 1:1,000,000. Patch tests with undiluted old tuberculin elicited strongly positive eczematous reactions. Complete blood counts and differential counts were normal. Examination showed the urine to be negative. Roentgenograms of the lungs showed old central tuberculous foci with healed nodes and moderate secondary thickening of the root branches. The Wassermann and Kline tests of the blood were negative.

On December 15 (twenty-five days after the second mass had been removed) another recurrent mass was removed. Inoculation of animals with this material failed to produce tuberculosis.

Generalized exposures to ultraviolet radiation and several intravenous injections of neoarsphenamine, a total of 1.25 Gm. having been given, produced no improvement. The patient has received three applications of filtered roentgen rays of 1 skin unit (280 roentgens) each to the affected area. The lesion has improved considerably.

NOTE.—Histologic examination proved the lesion to be tuberculous.

DISCUSSION

DR. GEORGE C. ANDREWS: This patient's history is much like that of several patients whom I have seen who had actinomycosis, which often starts after the extraction of carious teeth. The sudden onset is more in favor of actinomycosis than of tuberculosis. The organisms are often difficult to demonstrate. If the condition recurs I recommend that cultures be made for Actinomyces. Some cases of actinomycosis respond readily to roentgen treatments.

In my book there is the picture of a patient proved to have actinomycosis who was permanently cured by 1 filtered erythema dose. Of course, this is unusual. My experience has shown that many patients are incurable by any method of treatment.

DR. LUDWIG OULMANN: Dr. Eller mentioned that the condition was caused by trauma by a dentist. If it is tuberculosis, the dentist had nothing to do with it. Tuberculosis as well as other lesions appear after trauma when there is a systemic infection.

LUPUS ERYTHEMATOSUS WITH BULLOUS LESIONS. Presented by DR. ISADORE ROSEN.

This white man, aged 39, was presented before the Section on Dermatology of the New York Academy of Medicine in January 1932. Since 1932 he has had only intermittent treatment, receiving occasional injections of a bismuth preparation. Recently, after a flare-up of a peptic ulcer for which he was operated on a few years ago, the local condition became worse than ever. The eruption now involves practically the entire scalp and face, and there are very adherent scales and crusts together with scattered vesiculobullous lesions. The sister of the patient had lupus erythematosus, and the lesions cleared up with local applications of a bismuth preparation.

DISCUSSION

DR. JOSEPH J. ELLER: It is true that in some cases lupus erythematosus becomes distinctly worse after injections of a gold compound.

DR. ANDREW J. GILMOUR: I have never seen bullous lesions flare up after injections of a gold compound.

DR. MIHRAN B. PAROUNAGIAN: I saw this patient last year. He had an extensive eruption, but I do not recall any bullous lesions.

DR. GEORGE C. ANDREWS: I had a patient with an acute disseminated type of lupus erythematosus whose case is brought to mind by the one just presented. The results of a salt-poor diet in my patient were remarkable. The only other treatment was the application of boric acid compresses and rest indoors for about six weeks. The patient gained 18 pounds (8.2 Kg.), and the skin eruption entirely cleared. I have seen him occasionally since, and there have been slight relapses; but the results of this diet were so splendid that I wish to call attention to it as a possible method of treatment for the patient presented by Dr. Rosen.

DR. FRED WISE: Does the presenter believe that it would be unwise to treat this patient with a gold compound, starting with very small doses and gradually increasing them, and also to try bismuth preparations?

DR. ISADORE ROSEN: There was a marked improvement while the patient was receiving colloidal bismuth ointment locally and a bismuth preparation intramuscularly. He was presented because of the association of bullous lesions with discoid lupus erythematosus.

DERMATITIS HERPETIFORMIS (?) IN A SYPHILITIC PATIENT. Presented by DR. FRED WISE.

This man, aged 38, first applied for treatment at the clinic of the New York Post-Graduate Medical School and Hospital on Nov. 2, 1933. At that time he presented on the trunk a number of oval lesions, varying in diameter from one-fourth to one-half inch, and there were a few circular lesions on the extremities. The borders of the lesions showed evidence of faint vesiculation and superficial scaling. The eruption had been present for "several weeks."

Examination for fungi gave negative results. The Wassermann and Kline tests were strongly positive. Histologic examination of one of the lesions revealed merely a "superficial exudative inflammatory process." Routine antisyphilitic treatment has not influenced the rash.

The skin now exhibits slightly infiltrated, pinkish plaques, most of them circular and about one-fourth inch in diameter, showing a tendency to grouping. There is no evidence of vesiculation, but slight scaling is manifest, together with considerable inflammation from scratching. The lesions appear most pronounced on the upper parts of the arms, the thighs and the lower part of the back. The buccal mucosa is unaffected.

DISCUSSION

DR. MAX SCHEER: The eruption, especially on the thighs, resembles somewhat pityriasis rosea. I do not think that it is Duhring's disease.

DR. ANDREW J. GILMOUR: I agree with Dr. Scheer.

DR. MIHRAN B. PAROUNAGIAN: The duration of the eruption speaks against pityriasis rosea, and until there is a better diagnosis I accept that of Duhring's disease.

DR. LUDWIG OULMANN: I am rather inclined to agree with Dr. Wise. The grouping and the appearance of the papular lesions suggest dermatitis herpetiformis, but the case has to be worked out more thoroughly to verify the diagnosis.

DR. GEORGE C. ANDREWS: I agree with the presenter's diagnosis on account of the grouping and localization. The lesions in the axilla are decidedly edematous.

DR. HOWARD FOX: I agree entirely with the views expressed by Dr. Parounagian.

CHICAGO DERMATOLOGICAL SOCIETY

MAX S. WIEN, M.D., *Secretary*

Regular Meeting, April 18, 1934

JAMES H. MITCHELL, M.D., *President, Presiding*

ERYTHEMA (BULLOUS MULTIFORM). Presented by DR. M. H. EBERT and DR. B. B. BEESON.

This Negro, aged 43, entered the Cook County Hospital on March 28, 1934, with a history of blisters on the backs of the wrists, which were spreading to the forearms and hands. At that time he presented a rapidly spreading bullous eruption, with one small erosion on the hard palate. The bullae were large and appeared on apparently normal skin. The Nikolsky sign was not elicited, and there was generalized adenopathy. He had had a temperature of from 100 to 105 F.

A differential white blood cell count showed: polymorphonuclears, 44 per cent; lymphocytes, 34 per cent, and eosinophils, 22 per cent.

In the past few days the condition has improved considerably, and the patient now presents large, crusted erosions on the dorsa of the hands, fingers, wrists, elbows, knees, ankles and feet. The neck and the scalp are also involved, and there are scattered lesions on the trunk. The mucous membranes are free.

DISCUSSION

DR. UDO J. WILE: Judging from the history and the temperature chart, I think that the patient has what writers used to call "infectious pemphigus" or "butcher's pemphigus." I have seen a few cases of this malady, and the majority of the patients have died. The organism concerned has commonly been a hemolytic streptococcus. It might be interesting in this case to make blood cultures to determine whether there is a septic basis for the bullous eruption.

DR. PAUL A. O'LEARY: I think that the patient presents the severe erythema multiforme which is seen frequently in colored persons in the Cook County Hospital.

DR. MAX S. WIEN: This case is an example of a condition other instances of which have been observed at the Cook County Hospital. The question has always arisen in these cases as to whether the disease was acute (butcher's) pemphigus or erythema bullosum. My associates and I have considered it as belonging in the erythema bullosum group since all the patients recovered from their acute attacks. Although some of them have returned with remissions the disease has not followed the rapid fatal course of butcher's pemphigus. This man is considerably better than he was a few weeks ago and is apparently going to recover from the attack. I do not recall seeing a true case of acute (butcher's) pemphigus in the Cook County Hospital.

DR. M. H. EBERT: We have always been very much interested in cases of this type, and there are, relatively speaking, a large number of them. All the patients seem to be toxic, and we have not been able to find the cause. In this case blood cultures have not been made, but they were in other cases and were always negative. I hope that we shall be able to append the results of the serologic test for pemphigus when the report is published.

NOTE.—On May 19, 1934, only a few erosions persisted. The patient's general condition was excellent and he had had no new lesions for some time.

PITYRIASIS RUBRA (DEVERGIE'S DISEASE). Presented by DR. M. H. EBERT and DR. B. B. BEESON.

This Negro, aged 64, was admitted to the dermatologic service of the Cook County Hospital on April 8. He states that his skin was normal until three

months ago, when he noticed that an area on the left side of his face had become thickened, dry, scaly and whitish. Within two months, through successive involvement of scattered areas, his entire body became similarly affected. He feels well except for slight pruritus.

The skin is universally dry and scaling. On close inspection of the trunk, one can see that the individual lesions are acuminate, keratotic, follicular papules, and the skin has a nutmeg-grater texture. The cheeks, ears, end of the nose and scalp are covered with material which resembles mortar. Large, flaky scales are exfoliating below the elbows and knees. The palms and soles are hard and thick and feel like a carapace.

The basal metabolic rate was —7.

DISCUSSION

DR. RUBEN NOMLAND: This man probably has pemphigus foliaceus. In the first place, the condition is clinically similar to that of another patient in the hospital who has been proved by biopsy to have pemphigus foliaceus. I saw him several days ago, and at that time he had on the back several areas in which the epidermis was denuded and which I took to be a spontaneous Nikolsky sign.

DR. THEODORE CORNBLEET: I have attempted several times to elicit the Nikolsky sign but have never obtained it. It may be present at times, as Dr. Nomland said. I do not favor the diagnosis of pemphigus foliaceus as much as that of erythema toxicum.

DR. L. M. WIEDER: I suggest a diagnosis of a variant of keratosis follicularis. The skin is unlike that of pemphigus foliaceus in that much of the process is made up of finely follicular papules, although in general the skin feels harsh and dry as in Darier's disease. However, the papillomatous involvement of the alae nasi and other parts as well as the eroded area of the scapular region in which the process is most active might fit in with the clinical picture of atypical keratosis follicularis.

DR. M. H. EBERT: I think that the condition is Devergie's disease but that instead of being pityriasis rubra pilaris it is pityriasis nigra pilaris. That disease at times starts acutely and becomes generalized within a few weeks or months. On this patient's chest there are acuminate papules, and the peculiar mortar-like appearance of the scales on the nose and scalp is characteristic. The patient does not have keratotic plugs on the phalanges, but those are not invariably present in pityriasis nigra pilaris.

A CASE FOR DIAGNOSIS (PARAKERATOSIS VARIEGATA?). Presented by DR. S. W. BECKER.

This white man, aged 29, states that his skin has always been dry. At the age of 12 there developed pruritic lesions, at first limited to the arms, hands and legs, which gradually spread to the body. The condition is more extensive at present than at any previous time.

Over the upper and lower extremities and, to a small extent, on the trunk there are violaceous, scaling papules from 1 to 2 mm. in diameter, which have become confluent, forming large plaques, especially over the lower extremities. Some of the older lesions appear to be somewhat atrophic and hyperpigmented.

The Kolmer and the Kahn reaction of the blood serum were negative, and the urine was normal.

Microscopic section showed thickened and loose stratum corneum, stratum mucosum of normal thickness, with intercellular edema in the deeper portions, and some cellular infiltration. The chief changes were in the subpapillary portion of the dermis, consisting of rather marked cellular infiltration of small round cells, histiocytes and fibroblasts.

DISCUSSION

DR. UDO J. WILE: I think that the condition may be an unusual form of parapsoriasis. In my experience, most cases of parapsoriasis are hard to define.

Each seems to differ a little from the others, but they all have certain underlying characteristics, which this case shows. One should bear in mind that parapsoriasis may persist as such for several years and then granuloma fungoides may develop.

DR. H. R. FOERSTER: One is inclined to stress the subjective symptoms too much in cases of this type. The clinical picture is that of parakeratosis variegata, which I believe the condition to be even though there is complaint of pruritus.

DR. S. W. BECKER: I think that the condition is best classified as parakeratosis variegata, although I cannot exclude the possibility of lichenoid dermatitis, which is at times followed by atrophy. I have observed one case of parapsoriasis en plaques in which the lesions were cleared up by the treatment used by my associates and me for psoriasis, and I shall endeavor to treat this man by the same method.

MELANOSIS (POSTINFLAMMATORY, FOLLOWING BITES BY CIMEX LECTULARIUS)? URTICARIA PIGMENTOSA? Presented by DR. S. W. BECKER.

This boy, aged 6 years, blond, presents on both extremities, brown macules, varying from 3 to 10 mm. in diameter, which are said to have been present since the age of 6 weeks. At that time urticarial wheals developed, each of which was followed by the pigmented lesions. The mother does not believe that they could have been due to bedbugs.

On the upper and lower extremities are yellowish-brown macules, arranged in pairs, in groups of three and, in one instance, in a regular arc of five lesions.

A histologic section showed an increase in epidermal pigment.

DISCUSSION

DR. UDO J. WILE: How does Dr. Becker differentiate this condition clinically from urticaria pigmentosa?

DR. S. W. BECKER: My associates and I considered urticaria pigmentosa, flat pigmented nevi and postinflammatory melanosis. We were not able to produce a wheal by friction with a wooden tongue blade, which is sufficient to produce wheals in urticaria pigmentosa. The section showed slight perivascular infiltration with a moderate increase in epidermal melanin. There were no basophilic cells.

When the child was first seen the history was given that he was born with the lesions. Owing to their peculiar configuration we felt that they were probably factitious, and on further consultation with the family we learned that they began to develop when the patient was 6 weeks old, new ones appearing each morning, and that they were treated by local applications. The brownish lesions have persisted since that time, and wheals have never developed spontaneously. We thought that the distribution on the extremities was against the diagnosis of urticaria pigmentosa.

An interesting point is that the boy is a blond. It seems that certain persons, regardless of their complexion, have a tendency to acquire melanotic lesions after certain inflammatory conditions. I recall one or two patients presented before this society who had had similar lesions for several years following one of the exanthems.

DR. J. H. MITCHELL: I think that the urtication in this case is unmistakable. Perhaps it requires a Yale lock key to produce it, but the lesions became definitely urticated after a small amount of friction with a key.

DR. H. R. FOERSTER: If the condition were a persistent pigmentation following insect bites the lesions would be rounded; but they are all definitely oval and have other features commonly seen in urticaria pigmentosa, which I believe the malady to be.

DR. PAUL A. O'LEARY: In cases in which the pathologic picture does not confirm the clinical impression of urticaria pigmentosa the condition may be urticaria with pigmentation, in contradistinction to urticaria pigmentosa.

A CASE FOR DIAGNOSIS (KERATODERMIA BLENNORRHAGICA?). Presented by DR. THEODORE CORNBLEET and DR. EARLE R. PACE.

This American man, aged 19, was first seen yesterday. He presents an eruption on the lower extremities which, he states, began three years ago and has gradually developed to the present picture.

The eruption involves both lower extremities from the midportions of the thighs to the feet, extending slightly onto the soles, and consists of dusky red, elevated, sharply marginated keratodermic lesions, varying in size from that of a coin to half that of a palm; a few are definitely vegetating. Repeated questioning has failed to elicit a history of gonorrhea, and there is no physical evidence of such an infection. There are no punctate or conical keratoses on the palms or soles. No history suggestive of the ingestion of arsenic or of a halogen could be obtained.

DISCUSSION

DR. UDO J. WILE: I cannot get away from the impression that the condition looks like a nodular eruption due to bromide. I questioned the patient carefully, and he denied taking any bromide. However, Wise and Sulzberger recently called atttention to the fact that absence of a history of ingestion of bromine in a case of suspected bromoderma must be taken with reservations, since in certain states white flour is bleached with sodium bromate and enough bromine remains in the flour to produce an exanthem. It might be wise to test this patient to see if bromine can be recovered in the urine.

DR. THEODORE CORNBLEET: The patient denies taking any drugs, but that, of course, does not vitiate the possibility that he is getting iodine or bromine in some other way than in medicine. He has told me on several occasions that he has not had gonorrhea.

NOTE.—Iodine or bromine was not found in the urine. The patient has been treated with 5 per cent ammoniated mercury ointment and in three weeks has shown marked improvement.

Biopsy showed: The epidermis was irregularly acanthotic and showed many papillary projections. The rete pegs showed occasional widening and fusion. There was a moderate degree of intercellular edema, and many mitotic figures were present. The granular layer was discontinuous. The scale was very thick and nearly altogether parakeratotic. In the papillary and subpapillary layers the blood vessels were widely dilated and surrounded by a diffuse infiltration of lymphocytes, histiocytes and, in lesser numbers, plasma cells.

Directory of Dermatologic Societies *

INTERNATIONAL

Ninth International Congress of Dermatology and Syphilology

American Secretary: Dr. Howard Fox, 140 E. 54th St., New York.
Place: Budapest, Hungary. Time: Sept. 15-21, 1935.

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

W. R. Jaffrey, President, 64 Hughson St., S., Hamilton, Ont.
Basil Bowman, Secretary-Treasurer, 408 Medical Arts Bldg., Hamilton, Ont.
Place: Montreal, Quebec. Time: May 4, 1935.

Royal Society of Medicine, Section of Dermatology

Henry MacCormac, President, 23, Wimpole St., W. 1, London.
W. N. Goldsmith, Secretary, 6, Upper Wimpole St., W. 1, London.

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

Jeffrey C. Michael, Chairman, 1215 Walker Ave., Houston, Texas.
Harry R. Foerster, Secretary, 208 E. Wisconsin Ave., Milwaukee.
Place: Atlantic City. Time: June 10-14, 1935.

American Dermatological Association

Charles M. Williams, President, 114 E. 54th St., New York.
W. H. Guy, Secretary, 500 Penn Ave., Pittsburgh.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore-Washington Dermatological Society

Harry F. Anderson, President, 1610, 20th St. N.W., Washington, D. C.
Joseph V. Kennedy, Secretary, 1835 Eye St., Washington, D. C.

Central States Dermatological Association

Joseph Brumberg, President, 528 Delaware Ave., Buffalo.
William F. Hoover, Secretary, 333 Linwood Ave., Buffalo.
Place: Buffalo. Time: 1934.

Iowa and Western Illinois Dermatological Association

J. C. Kessler, President, University Hospital, Iowa City.
Robert E. Jameson, Secretary, 1014 First National Bank Bldg., Davenport, Iowa.

New England Dermatological Society

Rudolph Jacoby, President, 270 Commonwealth Ave., Boston.
J. Harper Blaisdell, Secretary, 45 Bay State Road, Boston.

Southern Medical Association, Section on Dermatology and Syphilology

Thomas W. Murrell, Chairman, 17 E. Grace St., Richmond, Va.
C. C. Dennie, Secretary, Professional Bldg., Kansas City, Mo.
Place: San Antonio, Texas. Time: November, 1934.

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

STATE DERMATOLOGIC SOCIETIES

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

Ernest K. Stratton, Chairman, 490 Post St., San Francisco.
John M. Graves, Secretary, 909 Hyde St., San Francisco.

Florida Society of Dermatology and Syphilology

Chairman for each meeting is elected from city in which meeting is held.
J. J. Saxton, Secretary, 205 Zack St., Tampa.

Louisiana Dermatological Society

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, Maison Blanche Bldg., New Orleans.

Medical Society of the State of New York, Section on Dermatology and Syphilology

George M. MacKee, Chairman, 200 W. 59th St., New York.
Lopo de Mello, Secretary, Medical Arts Bldg., Syracuse.

Medical Society of the State of Pennsylvania Section on Dermatology

Robert L. Gilman, Chairman, 1930 Chestnut St., Philadelphia.
Fred M. Jacob, Secretary, 7026 Jenkins Arcade Bldg., Pittsburgh.

Michigan State Medical Society, Section on Dermatology and Syphilology

A. R. Woodburne, Chairman, 26 Sheldon Ave., Grand Rapids.
G. Warren Hyde, Secretary, 2501 W. Grand Blvd., Detroit.

Minnesota Dermatological Society

D. D. Turnacliff, President, 407 Medical Arts Bldg., Minneapolis.
L. H. Winer, Secretary, 522 Medical Arts Bldg., Minneapolis.
Time: First Wednesday in October, December, February and April.

Oklahoma State Dermatological Society

C. L. Brundage, President, 1200 N. Walker St., Oklahoma City.
M. M. Wickham, Secretary, 716 W. Symmes St., Norman.

Texas Dermatological Society

C. F. Lehmann, President, 303 E. Houston St., San Antonio.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.

LOCAL DERMATOLOGIC SOCIETIES

Atlanta Dermatological Society

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

Bronx Dermatological Society

Louis Chargin, Chairman, 1 W. 85th St., New York.
Henry Silver, Secretary, 290 West End Ave., New York.

Brooklyn Dermatological Society

Arthur Persky, President, 1750 Ocean Parkway, Brooklyn.
George F. Price, Secretary, 884 Lincoln Place, Brooklyn.
Time: Third Monday of each month except June, July, August and September.

Buffalo-Rochester Dermatological Society

Earl D. Osborne, President, 471 Delaware Ave., Buffalo.
Richard L. Saunders, Secretary, 33 Linwood Ave., Buffalo.

Chicago Dermatological Society

James H. Mitchell, President, 25 E. Washington St., Chicago.
Max S. Wien, Secretary, 104 S. Michigan Ave., Chicago.

Cincinnati Dermatological Society

Samuel Goldblatt, President, 3208 Colerain Ave., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

Cleveland Dermatological Society

R. E. Barney, President, 1021 Prospect Ave., Cleveland.
E. W. Netherton, Secretary, 2020 E. 93d St., Cleveland.

Detroit Dermatological Society

Clyde K. Hasley, President, 1553 Woodward Ave., Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.

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Moses Scholtz, Chairman, 1930 Wilshire Blvd., Los Angeles.
Nelson P. Anderson, Secretary, 2007 Wilshire Blvd., Los Angeles.

Manhattan Dermatologic Society

Louis B. Mount, Chairman, 256 State St., Albany, N. Y.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

Montreal Dermatological Society

Alberic Marin, President, 1414 Drummond St., Montreal, Canada.
Paul Poirier, Secretary, 2073 St. Denis St., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

Ray H. Rulison, Chairman, 145 E. 54th St., New York.
E. William Abramowitz, Secretary, 853, 7th Ave., New York.

New York Dermatological Society

Fred Wise, President, 200 W. 59th St., New York.
R. H. Rulison, Secretary, 145 E. 54th St., New York.

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J. W. Hellwig, Chairman, 1319 Farnam St., Omaha.
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Robert L. Gilman, Chairman, 1930 Chestnut St., Philadelphia.
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J. Cavanaugh, Secretary, 28 Market St., Youngstown, Ohio.

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Richard S. Weiss, President, 3720 Washington Blvd., St. Louis.
M. F. Engman, Jr., Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

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CONTENTS

Identity of a Streptococcus Isolated from Patients with Pemphigus: Preliminary Report. Preston A. Welsh, M.D., Rochester, Minn. 643

Mucha-Habermann Syndrome (Parapsoriasis en Plaques Disseminées): A Critical Study with a Report of Cases. Moses Schorr, M.D., Los Angeles 653

Dermatitis Venenata from Rhus Toxicodendron: Report of Individual Cases. F. Ronchese, M.D., Providence, R. I. 665

Epithelioma Adenoides Cysticum. Franz Schuler Jr., M.D., Ann Arbor, Mich. 667

Mucous Cysts of Fingers. H. Sutherland Campbell, M.D., and [illegible], Ph.D., Los Angeles 674

Vaginismus: A Review. Joseph Goodman Jr., M.D., and Arthur M. Greenwood, M.D., Boston 689

Arsphenamine Dermatitis: Attempted Sensitization to Neoarsphenamine and Further Observations on the Fever Test. Arthur C. Schoch, M.D., Dallas, Texas 692

Value of Organic Luetin in Diagnosis and Treatment of Syphilis: A Study of Nine Hundred Cases. Leslie P. [illegible], M.D., New York 696

The Safety of Lumbar Puncture for Ambulatory Patients. Harold C. Torrey, M.D., San Francisco 692

Clinical Spectroscopy: The Quantitative Estimation of Nickel in Psoriasis. L. Edward Gaston, M.D., and A. H. Straus, B.S., New York 697

Acute Pemphigus: Report of Case Occurring in Granulocytopenia. M. J. Fiala, M.D., Dubuque, Iowa 704

Multiple Idiopathic Hemorrhagic Sarcoma (Kaposi): Report of a Case in an American Negress. Francis A. [illegible], M.D., Baltimore 706

Neurodermitis Chronica 709

Abstracts from Current Literature 710

Society Transactions:

Cleveland Dermatological Society 719

Los Angeles Dermatological Society 726

Bronx Dermatological Society 734

New York Dermatological Society 746

Manhattan Dermatologic Society 751

Chicago Dermatological Society 754

Directory of Dermatologic Societies 758